

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 21-691 (GBW)
	)	
AVADEL CNS PHARMACEUTICALS LLC,	)	
	)	
Defendant.	)	Redacted - Public Version

JAZZ PHARMACEUTICALS, INC. and	)	
JAZZ PHARMACEUTICALS IRELAND	)	
LIMITED,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. 21-1138 (GBW)
	)	
AVADEL CNS PHARMACEUTICALS LLC,	)	
	)	
Defendant.	)	Redacted - Public Version

JAZZ PHARMACEUTICALS, INC. and	)	
JAZZ PHARMACEUTICALS IRELAND	)	
LIMITED,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. 21-1594 (GBW)
	)	
AVADEL CNS PHARMACEUTICALS LLC,	)	
	)	
Defendant.	)	Redacted - Public Version

**PLAINTIFFS' OPENING BRIEF IN SUPPORT OF
RENEWED MOTION FOR A PERMANENT INJUNCTION**

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I. INTRODUCTION

The injunction is back on remand because Avadel volleyed a plethora of new objections to it for the first time on appeal. The injunction preventing Avadel from marketing, making, using, or selling Lumryz for the treatment of idiopathic hypersomnia (“IH”) through the February 18, 2036 expiration of U.S. Patent No. 11,147,782 (the “’782 patent”) remains. The issue now before this Court is whether it should again enjoin Avadel from seeking approval for IH before February 19, 2036 to prevent Avadel from violating the injunction. The factual record, not developed for the Federal Circuit because Avadel never raised the issue below, confirms a causal nexus exists between Avadel seeking approval for IH and the harm to Jazz. Enjoining Avadel from seeking approval is necessary to give effect to the Court’s injunction, and Avadel must ensure it does not receive approval for IH during the term of the injunction.

Avadel has indicated its request to the FDA for IH approval is imminent. Once Avadel requests approval, nothing stops the FDA, a non-party to this action that cannot be enjoined in this case, from approving Avadel’s request (which Avadel has represented will happen swiftly). Indeed, despite the Federal Circuit positing that Avadel may not pursue its IH indication for financial reasons or lack of success in its studies, Avadel has repeatedly publicly stated that it is rapidly pursuing this multi-billion-dollar opportunity and that its clinical study is on track. It did so in a statement as recently as May 7, 2025, after the Federal Circuit issued its opinion.

Because FDA approval would require Avadel to add the IH indication to the Lumryz label, FDA approval of Lumryz to treat IH inevitably would lead to the sale and use of Lumryz to treat IH, expanding the scope of Avadel’s infringement and causing further irreparable harm to Jazz, whose Xywav[®] product is the only approved product for the treatment of IH. Such labeling—long considered a form of marketing that will induce physicians to infringe—would tell prescribers and patients Lumryz is safe and effective for IH. It also would result in insurance coverage for IH,

which would greatly increase its infringing use. Such harm cannot be compensated monetarily. Because Avadel cannot market, make, use, or sell Lumryz for IH, it will suffer no hardship from the requested injunction, which would only require that Avadel ensure that it does not receive approval for IH before the '782 patent expires. For the same reason, the proposed injunction will not harm the public interest. In fact, on appeal, Avadel repeated its arguments against the remaining *eBay* factors, and the Federal Circuit “considered [those] arguments and [found] them unpersuasive.” *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, 136 F.4th 1075, 1089 (Fed. Cir. 2025) (“CAFC Op.”). The Court should grant the relief requested herein.

II. NATURE AND STAGE OF THE PROCEEDINGS

Prior to trial, Avadel stipulated to infringement of claim 24 of the '782 patent. D.I. 550.¹ After a five-day trial, the jury rejected Avadel's invalidity challenges. D.I. 579 at 8-11. Jazz requested a limited permanent injunction and an ongoing royalty (D.I. 586-589, 610-612), which Avadel opposed (D.I. 601-609). On August 27, 2024, this Court granted-in-part a limited permanent injunction and enjoined Avadel from “seeking approval from the [FDA] and marketing Lumryz for the treatment of IH” and “from infringing in any way Claim 24 of the '782 patent, by making, using, or selling Lumryz or any product not more than colorably different from Lumryz, through and including the expiration date of the '782 patent.” D.I. 666 at 2-3. The Court also issued factual findings and analysis supporting its conclusions. D.I. 665.

Avadel appealed the injunction order the next day (D.I. 667), and requested an emergency stay of the injunction on September 3, 2024 (D.I. 670). This Court issued an order denying the stay and clarifying the scope of the injunction (D.I. 710), which Avadel also appealed (D.I. 712). The stay order clarified that “while the Order enjoins Avadel from seeking FDA approval for IH,

¹ All “D.I.” references refer to docket entries in C.A. No. 21-691 unless otherwise identified.

the Order does not enjoin Avadel from *submitting information or results* from ongoing clinical studies to the FDA.” D.I. 710 at 4 (emphasis in original). The Federal Circuit issued a stay only with respect to “initiating new clinical trials or studies.” D.I. 714 at 3.

The Federal Circuit reversed-in-part (as related to clinical trials and the open-label extension) and vacated-in-part the injunction and remanded to this Court to make additional factual findings and determine whether enjoining Avadel from requesting FDA approval for an IH indication is necessary to prevent infringement and to re-address the *eBay* factors accordingly. CAFC Op. at 1088-89. The Federal Circuit found factual support for, and did not disturb, the portion of the injunction preventing Avadel from marketing, making, using, or selling Lumryz for IH through expiration of the ’782 patent. *Id.* at 1089; D.I. 733 at 1.

III. THE COURT SHOULD ENJOIN AVADEL FROM REQUESTING FDA APPROVAL FOR A LUMRYZ IDIOPATHIC HYPERSOMNIA INDICATION

An injunction preventing Avadel from seeking FDA approval for IH is “necessary to prevent future infringement” in the IH population. CAFC Op. at 1089; *see also Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342, 1367 (Fed. Cir. 1998) (explaining an injunction may reach non-infringing activities, where “[i]t is necessary ... that the injunction prevent infringement” of a patent). The Federal Circuit held that “the submission of an application to the FDA is not infringement under § 271(a)” and “is not an activity that triggers the safe harbor.” CAFC Op. at 1086. But “it was not improper for [this] court to consider whether enjoining Lumryz from engaging in that activity was warranted based on a full consideration of the *eBay* factors” if enjoining that activity is “necessary to prevent infringement” and there exists a “causal nexus” between Jazz’s irreparable harm and Avadel requesting IH approval. *Id.* at 1088-89 (internal citations omitted). As explained herein, an injunction preventing Avadel from requesting FDA approval for IH is necessary to prevent the harms this Court has recognized Jazz would suffer if

Lumryz is marketed, made, used, or sold for IH prior to the expiration of the '782 patent. The Federal Circuit already considered and found unpersuasive Avadel's other *eBay* factor arguments (*id.* at 1089); those factors, thus, too support enjoining Avadel from requesting IH approval.

A. Enjoining Avadel From Requesting FDA Approval For IH Is Necessary To Prevent Currently Enjoined Infringement And Irreparable Harm To Jazz

Courts “may grant injunctions in accordance with the principles of equity to prevent the violation of any right secured by patent, on such terms as the court deems reasonable.” 35 U.S.C. § 283. This Court possesses “broad discretion to determine how best to enforce its injunctive decrees.” *TiVo Inc. v. EchoStar Corp.*, 646 F.3d 869, 881 (Fed. Cir. 2011).

A court granting an injunction may “not properly deny the one element of such relief that [would be] necessary to make it effective.” *Trans-World Mfg. Corp. v. Al Nyman & Sons, Inc.*, 750 F.2d 1552, 1564 (Fed. Cir. 1984); *Joy Techs., Inc. v. Flakt, Inc.*, 6 F.3d 770, 777 (Fed. Cir. 1993) (“The new injunction may enjoin Flakt’s acts which constitute direct, induced or contributory infringement during the term of the patent . . . [as well as such] additional conditions [as] are necessary to ensure that Flakt does not enable direct infringement [by others].”); *Kaspar Wire Works, Inc. v. K-Jack Eng’g Co.*, No. 95-1095, 1995 WL 662674, at *3 (Fed. Cir. Nov. 9, 1995) (rejecting argument that “district court may do no more than is strictly necessary to prevent further acts of direct infringement by the enjoined party”). To ensure that an injunction is effectual, “otherwise permissible practices connected with the acts found to be illegal must sometimes be enjoined.” *United States v. Loew’s, Inc.*, 371 U.S. 38, 53 (1962).

In the patent context, an injunction may reach activities that “do not themselves constitute infringement,” so long as it is necessary to prevent infringement. *Johns Hopkins Univ.*, 152 F.3d at 1366; *Nat’l Instruments Corp. v. Mathworks, Inc.*, 113 F. App’x. 895, 898-99 (Fed. Cir. 2004) (affirming injunction barring all sales of accused product where “[t]he trial court was cognizant

[that there may be non-infringing uses] and nonetheless determined that ‘the scope of the injunction remains that which is necessary to deter future infringement’”) (cite omitted); *Smith & Nephew, Inc. v. Synthes (U.S.A.)*, 466 F. Supp. 2d 978, 988 (W.D. Tenn. 2006) (“A district court . . . can enjoin activities that ‘do not themselves constitute infringement’ if necessary to prevent infringement.”); *Brooktrout, Inc. v. Eicon Networks Corp.*, No. 03-59, 2005 WL 8160605, at *4 (E.D. Tex. Jul. 25, 2005) (“A court is justified in issuing such relief [of enjoining non-infringing conduct] if the court is persuaded that such a ban is necessary to stop future infringement even though the order has the ancillary effect of preventing some lawful uses.”); *Glob. Traffic Techs. LLC v. Tomar Elecs., Inc.*, No. 05-756, 2009 WL 10678424, at *14 (D. Minn. Jan. 22, 2009) (enjoining accused product despite non-infringing uses being “theoretically possible” because “[t]o do otherwise would leave [patentee] exposed to a large risk of future infringement by [infringer] and not give adequate enforcement to [patentee’s] patent rights”).

Here, Avadel’s appeal did not disturb the portion of the injunction that prevents Avadel from marketing, making, using, or selling Lumryz for IH through the expiration of the ’782 patent. D.I. 733 at 1. This Court is well within its discretion to narrowly enjoin Avadel from seeking FDA approval for that indication through patent expiration, because doing so is “necessary to make [the injunction] effective.” *Trans-World*, 750 F.2d at 1564.

The record evidence demonstrates the following four facts: (1) unless Avadel is enjoined from requesting FDA approval to treat IH, once Avadel’s trial is completed next year, Avadel will submit an application for IH; (2) Avadel expects the application will be swiftly approved; (3) an IH indication will be included on Lumryz’s label and Avadel will be marketing for IH, inducing physicians to prescribe and patients to use Lumryz for IH in violation of the injunction; and (4) Avadel admits that FDA approval will result in the current injunction being violated. *See*

GlaxoSmithKline LLC v. Teva Pharms. USA, Inc., 7 F.4th 1320, 1333-34 (Fed. Cir. 2021) (“Our precedent has consistently held that, when a product is sold with an infringing label or an infringing instruction manual, such a label is evidence of intent to induce infringement.”).

1. Avadel will submit an application for an IH indication

The Federal Circuit’s suggestion that “Avadel may decide the financial investment in pursuing the approval does not comport with its business prospects,” (CAFC Op. at 1089), lacks any support. Avadel’s public statements and actions prove otherwise.

One of Avadel’s primary goals is to expand Lumryz’s eligible patient population, which Avadel has publicly planned to do through additional indications since Lumryz launched in June 2023. PTX300.112-113. In the months leading up to and during trial, Avadel’s CEO Greg Divis reiterated that Avadel would be seeking an IH indication. PTX1899.8; D.I. 596, 2/27 Tr. (Divis) at 519-520, 529. And the day the jury found Avadel infringed a valid patent, knowing Avadel could still be enjoined from further infringement, Mr. Divis stated in an Avadel earnings call that “[t]he next growth opportunity we’re pursuing is LUMRYZ for the treatment of idiopathic hypersomnia or IH” and that Avadel was “currently well advanced in the planning stages to initiate a multicenter, randomized controlled trial for IH in the second half of this calendar year.” Ex. 2 at 3; *see also* D.I. 606, Divis Decl. ¶ 12-13. Since then, Avadel has steadily moved toward completion of its trial and has never wavered in its intention to submit an application. Ex. 3 at 5, 17 (post-injunction hearing, pre-injunction decision); Ex. 4 at 4 (post-injunction decision, pre-appellate decision); Ex. 5 (post-appellate decision); Ex. 6 at 8:5-13 (post-appellate decision). Avadel did not even pause its clinical trial efforts after representing to the Court at the June 2024 injunction hearing that it would not move forward if enjoined. Ex. 7 at 64:15-21; 86:1-8; Ex. 8. Avadel launched its clinical trial weeks later—prior to the Court’s injunction decision. Ex. 8.

In May 2025, following this remand, Avadel repeatedly stated that it is a foregone conclusion that it will seek to expand infringement of Jazz’s patent with Lumryz. Avadel said it “expect[s] to complete enrollment in the trial before the end of 2025 and are targeting top line data in the first part of 2026, followed by an NDA filing thereafter.” Ex. 6 at 8:10-13. Far from abandoning its efforts, which the Federal Circuit suggested, Avadel stated “it’s very clear and very straightforward that [the Federal Circuit’s] *vacatur* gives us a pathway to file and secure and seek FDA approval,” *id.* at 28:19-23 (emphasis added), absent an injunction from this Court. Avadel understands that as long as it can seek FDA approval, the current injunction will not prevent it from increasing and eventually profiting from infringing IH sales. *See Glob. Traffic*, 2009 WL 10678424, at *13 (enjoining all sales of infringing product despite non-infringing uses where infringer’s “only apparent reason to sell code-capable emitters is for eventual use in code-capable systems, which would itself constitute an act [of] infringement”).

Avadel’s investment in IH and continued belief in the significant financial opportunity IH presents show that it will not reverse course and “decide the financial investment in pursuing the approval does not comport with its business prospects,” CAFC Op. at 1089, but rather that it is “*relentlessly* committed to” receiving IH approval. Ex. 5 (emphasis added). In sum, Avadel sees IH as crucial to its success. Thus, even while faced with a potential injunction, Avadel made significant investments in an IH indication, including [REDACTED] [REDACTED] D.I. 606, Divis Decl. ¶ 12.

Avadel expects a significant return on this investment. “Avadel’s interest in the IH market stems from its recognition that the market holds ‘a lot of opportunity’ because ‘there’s a robust patient population . . . with only one currently FDA approved treatment, [Xywav].” D.I. 665 at 22 (quoting D.I. 591-1, Exhibit 2 at 23). Avadel estimates the number of patients with IH at 40,000

to 42,000. Ex. 10 at 21, 23; Ex. 6 at 8:14-20; Ex. 4 at 4; Ex. 11 at 6. Avadel also covets the IH market because of its nascency. See D.I. 665 at 22 (“Indeed, with FDA approval, Lumryz will compete head-to-head against Xywav in a newly-developing market.”). Xywav remains the only FDA-approved treatment for IH. D.I. 665 at 22; Ex. 6 at 8:14-18. And Avadel estimates that 90% of patients diagnosed with IH are not yet treated. Ex. 10 at 21. Avadel stresses that this is “a significant additional unrealized market opportunity” with “clear market potential” that is “highly untapped and ripe.” Ex. 6 at 8:14-20, 9:8-11, 21:11-15.

Avadel’s continued focus on the “significant additional unrealized market opportunity” IH presents refutes the Federal Circuit’s concern that “Avadel may decide the financial investment in pursuing the approval does not comport with its business prospects.” CAFC Op. at 1089. Instead, Avadel views expanding the eligible Lumryz population as “key to Avadel’s future growth and value creation.” Ex. 6 at 8:5-7.

2. Avadel expects the FDA to approve its request for Lumryz to treat IH

Avadel’s public statements and general course of FDA conduct demonstrate that, from Avadel’s point of view, the Federal Circuit’s suggestion that Avadel’s “[c]linical trials may fail” to result in FDA approval, CAFC Op. at 1089, lacks any factual support.

Avadel expects to seek approval for IH in early 2026 after completion of its phase 3 clinical trial. Ex. 6 at 8:5-13. On July 31, 2024, Avadel announced it had dosed the first patient in its phase 3 IH trial, which it calls “REVITALYZ.” Ex. 8. On May 7, 2025, Avadel stated that it “expect[s] to complete enrollment in the trial before the end of 2025 and [is] targeting top line data in the first part of 2026, followed by an NDA filing thereafter.” Ex. 6 at 8:5-13.

Avadel expects this single phase 3 study is sufficient for FDA approval, pointing to Jazz’s single study for Xywav in treating patients with IH to support Jazz’s application. Ex. 3 at 17; Exs. 12-13. Avadel’s own expert, Dr. Stern, opined that one phase 3 trial will suffice because he expects

Lumryz to be similarly efficacious to Xywav:

[T]here is no reason to think that sodium oxybate options, including Xyrem and Lumryz, would be any less effective than mixed-salts Xywav for treating idiopathic hypersomnia. In fact, sodium oxybate is noted in 2017 French guidelines to be potentially effective for the treatment of EDS and sleep inertia in idiopathic hypersomnia and is conditionally recommended for the treatment of idiopathic hypersomnia in the 2021 American Academy of Sleep Medicine guidelines. Although there have been no phase III randomized controlled trials, multiple published studies have evaluated sodium oxybate in idiopathic hypersomnia and shown that sodium oxybate therapy was associated with improved symptoms in IH patients.

D.I. 607, Stern Decl. ¶ 15.

Once Avadel's clinical trial is completed, Avadel expects the FDA to take about ten months to review Avadel's application. D.I. 672, Gudeman Decl. ¶ 10. By Avadel's timeline, the FDA would find Avadel approvable for IH by late 2026 or early 2027.

This Court cannot enjoin the FDA, a non-party to this litigation, from approving Avadel's IH application. *Ben Venue Lab's, Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 584 n.10 (D.N.J. 2001) ("Since the FDA is not a party to this suit, the Court lacks any jurisdiction over it."). Therefore, absent an injunction, the FDA will be free to approve once its review is complete. It is thus necessary to enjoin Avadel from requesting FDA approval to prevent Avadel from receiving approval for IH and expanding the scope of its already-enjoined infringement.

3. Upon approval for IH, the Lumryz label will include the IH indication, resulting in Avadel marketing and selling Lumryz for IH

As explained below, once Lumryz is approved to treat IH, the law requires that its labeling include that approved indication and be made public. At that point, Avadel will be marketing and selling Lumryz for IH, inducing physicians to prescribe and patients to use Lumryz for IH in violation of the injunction. *See GlaxoSmithKline LLC*, 7 F.4th 1320 at 1333-34; *see also Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1129 (Fed. Cir. 2018) ("The contents of the label itself may permit the inference of specific intent to encourage, recommend, or promote

infringement.”).²

a. Avadel’s application must include proposed labeling for IH which would become part of the labeling for Lumryz

The FDA’s labeling requirements ensure that any approval would result in Avadel inducing infringement. The FDA required Jazz to “submit proposed prescribing information (PI) [or labeling] that conforms to the content and format regulations.” Ex. 14 at 9. When the FDA approved Jazz’s IH application, it specifically referred to the proposed labeling. Ex. 15 at 1 (approving application “for use as recommended in the enclosed agreed-upon labeling”). The FDA informed Jazz that the final labeling “will be accessible from publicly available labeling repositories” and “request[ed] that the labeling approved today be available on [Jazz’s] website within 10 days.” Ex. 15 at 2; Cortez Decl. at ¶ 52. The same will apply to Avadel’s application.

Like Jazz, Avadel must submit proposed labeling with its application that includes the new IH indication and safety and efficacy information from Avadel’s IH trial. See 21 C.F.R. § 314.70(b)(2)(v) (labeling changes requiring supplemental NDA submission), § 201.56(c)(1) (“proposed conforming labeling must be submitted as part of the application”); 21 U.S.C. § 355(b)(1)(A)(vi) (requiring “specimens of the labeling proposed to be used for such drug”); Cortez Decl. at ¶¶ 13-15, 30-34. Avadel’s proposed labeling “*must* contain the specific information required under § 201.57(a), (b), and (c).” 21 C.F.R. § 201.56(d)(1) (emphasis added); § 201.56(b)(1)(iii) (“Prescription drug products for which an NDA . . . or efficacy supplement is submitted” are “subject to the labeling requirements in paragraph (d) of this section and

² The ’782 patent claims a unit dosage form. But Avadel is enjoined from, “making, using, or selling Lumryz” for uses other than treating narcolepsy patients. D.I. 666 at 2. Jazz is not required to prove inducement by Avadel. Jazz merely cites the above cases for the well-settled principle that disseminating drug product labeling instructing a specific use means that the company marketing that drug product is liable for causing infringement of that use.

§ 201.57.”); Cortez Decl. at ¶¶ 16, 41-46. Section 201.57(c)(2) requires Avadel to include information regarding the indications and usage of Lumryz in section one of its labeling, and Section 201.57(c)(15) requires Avadel to “discuss those clinical studies that facilitate an understanding of how to use the drug safely and effectively” including “the studies that support effectiveness for the labeled indication(s).” *See also* Cortez Decl. at ¶¶ 41-46. The FDA agrees that “[t]o comply with the general labeling requirements in 21 CFR 201.56 and 201.57, the INDICATIONS AND USAGE section *must . . . clearly convey the use(s) for which the drug has been shown to be safe and effective.*” U.S. Food and Drug Administration, Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products – Content and Format, Draft Guidance for Industry (July 2018), at 2 (available at <https://www.fda.gov/media/114443/download>). Thus, with its application, Avadel must propose labeling with an IH indication and information on efficacy and safety for IH.

Once approved, the proposed labeling will become the approved labeling for Lumryz. Ex. 15 at 1; Cortez Decl. at ¶¶ 29-34. It is thus necessary to enjoin Avadel from requesting FDA approval to prevent an IH indication on Avadel’s label. *See Brooktrout*, 2005 WL 8160605, at *6 (“enjoin[ing] Eicon from publishing any document to be distributed in the United States which contains any instructions to users explaining how to configure the Eicon Diva Server in a[n] infringing manner”).

b. Marketing and selling Lumryz with Avadel’s revised labeling will induce physicians and patients to use Lumryz to treat IH

Once IH is on the Lumryz label, Avadel will be marketing, making, using, and selling Lumryz for IH (despite the Court’s injunction). In fact, Avadel will be inducing physicians to prescribe and patients to use Lumryz for IH. Lumryz’s new label will be published by the FDA, listed on Avadel’s website, and included with Lumryz advertisements. Lumryz’s IH approval will

be publicized to investors, to physicians, and to pharmacy benefit managers (“PBMs”). These activities all result in the same irreparable harm this Court already found Jazz would suffer once Avadel commercializes Lumryz for IH. D.I. 665 at 3-11, 22-24; *see also infra* at 15-18.

The FDA *must* post Avadel’s approved labeling on its website so that healthcare providers and patients may access it. 21 U.S.C. § 355(r)(3) (requiring the FDA to “post on [its] Internet Web site . . . the approved professional labeling and any required patient labeling of a drug approved under this section” within 21 days of approval “including in a supplemental application with respect to a labeling change”); Cortez Decl. at ¶¶ 47-51.

Avadel must also “revise all promotional labeling and advertising to make it consistent with any labeling change.” 21 C.F.R. § 314.70(a)(4); Cortez Decl. at ¶ 35-40. Therefore, Avadel must include the IH indication in the labeling when it distributes Lumryz. Avadel’s new labeling will be included with Lumryz marketing materials and will be available to healthcare providers. Brief Summary and Adequate Directions for Use: Disclosing Risk Information in Consumer-Directed Print Advertisements and Promotional Labeling for Prescription Drugs, Draft Guidance for Industry (August 2015), at 3 (available at <https://www.fda.gov/media/70768/download>) (“Generally, the requirements in 21 C.F.R. 201.100(d) have been fulfilled by including the full FDA-approved package insert (PI) with promotional labeling materials.”); *see also* 21 CFR 314.81(b)(3)(i); Cortez Decl. at ¶ 36. These requirements are intended to disseminate the information in Avadel’s approved labeling to prescribers and patients. *See e.g.*, 21 U.S.C. § 355(r)(1) (requiring creation of website database for labels to “improve the transparency of information about drugs and *allow patients and health care providers better access to information about drugs*”) (emphasis added). Mandatory distribution of Lumryz’s label with an IH indication will wholly negate this Court’s injunction.

Federal Circuit precedent holds a label “instructing how to engage in an infringing use[] show[s] an affirmative intent that the product be used to infringe.” *GlaxoSmithKline LLC*, 7 F.4th at 1333-34; *see also Braintree Lab’ys. v. Breckenridge Pharm., Inc.*, 688 F. App’x 905, 910 (Fed. Cir. May 5, 2017) (Because the label “instructs how to engage in an infringing use, it shows an affirmative intent that the product be used to infringe.” (cleaned up)). Inclusion of IH on Lumryz’s label would demonstrate Avadel’s intent for physicians to prescribe and patients to use Lumryz for IH.

Avadel’s intent is further demonstrated by its continued public statements regarding IH since being enjoined. Avadel keeps investors apprised of its clinical trial, its investment in IH, and the size of the IH “opportunity.” *See supra* at 6-8. Avadel also continues to speak “directly [with] clinicians and leading key opinion leaders” regarding “the potential prospects of LUMRYZ and IH.” Ex. 11 at 6; Ex. 16 at 2; Ex. 4 at 4. And after approval, Avadel intends to disseminate its clinical trial data and IH indication “to the public at large.” No. 24-2274, D.I. 42 at 7, 31 (Fed. Cir. Nov. 13, 2024). Avadel’s public statements confirm its intent for healthcare providers to prescribe, patients to use, and Avadel to sell Lumryz for IH once approved.

Once approved, physicians will prescribe Lumryz for IH. Bogan Declaration at ¶¶ 15, 29-42. Dr. Lavender, an Avadel declarant for its opposition to Jazz’s original injunction, stated that “[a]s soon as [Lumryz] is approved for IH, I will offer it to my IH patients for whom it is appropriate.” D.I. 608, Lavender Decl. ¶¶ 11, 19. Even without that approval, Mr. Divis said “doctors are currently permitted to . . . prescribe LUMRYZ off-label for use in IH.” D.I. 606, Divis Decl. at ¶ 15. Avadel has recorded off-label sales. D.I. 671 at 15 (twenty IH patients taking in September 2024). Any non-narcolepsy sales with the current injunction are a violation.

c. Adding IH to Lumryz’s label will increase insurance coverage

Before the injunction, “the number of IH patients taking LUMRYZ off-label for IH [wa]s low because insurance coverage [wa]s not available for off-label use of LUMRYZ.” D.I. 606, Divis Decl. at ¶ 15. But if Lumryz is approved for IH, PBMs would cover it. Avadel says, “[o]nce [Avadel] get[s] approval, there should be insurance coverage for LUMRYZ for IH, and that is when [Avadel] expects to see more patients taking LUMRYZ for IH.” *Id.*; see also Ex. 9 at 2 (“Supplemental indication approval by the FDA is also critical for ensuring insurance coverage.”). Avadel intends to profit from IH sales: to obtain approval for IH, expand coverage, then purportedly passively allow doctors “to exercise their medical judgment and prescribe LUMRYZ . . . for use in IH.” D.I. 606, Divis Decl. at ¶ 15.

Avadel has already argued that the current injunction “does not and cannot control off-label use because *Avadel* does not and cannot control off-label use,” and “[t]o the extent a doctor chooses to prescribe a medication off-label, that is a choice between the physician and patient and is not subject to this Court’s injunction.” D.I. 671 at 15 (emphasis in original). But the infringing *making* and *sale* by Avadel for uses other than treatment of narcolepsy is a violation of the current injunction regardless of whether Avadel is actively promoting Lumryz for IH. And, Avadel obtaining FDA approval before the ’782 patent expires will induce direct infringement by physicians and patients in further violation of the injunction and the ’782 patent. This Court should, therefore, enter the requested injunction. *Joy Techs.*, 6 F.3d at 777 (approving injunction “necessary to ensure that Flakt does not enable direct infringement [by others]”).

4. Avadel admits FDA approval will result in violation of the injunction

Avadel stated during oral argument at the Federal Circuit that once Avadel receives IH approval and IH is on Lumryz’s label, the parties will “end up back in front of the district court, and we would sort it out there” and that “we would have to litigate it.” Ex. 17 at 30:25-32:13. But there is nothing left to litigate. Avadel stipulated that Lumryz infringes claim 24 of the ’782 patent.

D.I. 550. That claim is valid. D.I. 579. And Avadel is enjoined from marketing, making, using, or selling Lumryz for IH. D.I. 666 at 2-3; D.I. 733 at 1. Avadel has no reason to request FDA approval ten years in advance of when it can sell Lumryz for IH.

Any protest from Avadel that it will not actively market or sell for IH if approved rings hollow. The above analysis demonstrates that such marketing and sales for IH—resulting in Jazz’s irreparable harm—inevitably flows from FDA approval of Lumryz for IH. For Avadel to succeed on a no-risk-of-future-infringement argument, it must present “*evidence [that] is very persuasive that future infringement will not take place.*” *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 842 F.2d 1275, 1281-82 (Fed. Cir. 1988) (emphasis added). Avadel cannot present any such evidence. And as explained above, Avadel is required by law to market Lumryz under its approved labeling which will also be published by FDA and relied upon by PBMs, prescribers, and patients. At that point, the Court could not remedy the irreparable harm done to Jazz.

The Court must not “deny the one element of such relief that [would be] necessary to make [the injunction] effective.” *Trans-World*, 750 F.2d at 1564. Allowing Avadel to seek approval before February 19, 2036 would render the current injunction ineffective; enjoining Avadel from seeking approval is “necessary to ensure that [Avadel] does not enable direct infringement.” *Joy Techs.*, 6 F.3d at 777; *Kaspar Wire Works*, 1995 WL 662674, at *3.

B. The *eBay* Factors Support This Court Enjoining Avadel From Requesting FDA Approval For Lumryz To Treat Idiopathic Hypersomnia

1. Avadel’s request for approval of Lumryz to treat IH will cause Jazz irreparable harm

A patentee must prove “1) that absent an injunction, it will suffer irreparable harm, and 2) that a sufficiently strong causal nexus relates the alleged harm to the alleged infringement.” *Apple Inc. v. Samsung Elecs. Co. Ltd.*, 695 F.3d 1370, 1374 (Fed. Cir. 2012). This Court previously “agree[d] that Jazz would suffer irreparable injury if Avadel is not enjoined from seeking FDA

approval and marketing Lumryz for IH.” D.I. 665 at 22. The Federal Circuit found no fault in this Court’s findings that “‘Lumryz’s entrance into the IH market would undoubtedly cause Jazz to suffer significant injury’” because “[u]nlike the narcolepsy indication, . . . ‘Jazz’s Xywav is the only FDA-approved treatment for IH,’ and therefore, ‘Avadel’s entrance into the market would strip Jazz of a unique selling point critical to growing its reputation and goodwill.’” CAFC Op. at 1088-89 (quoting D.I. 655 at 22-23). It merely found them insufficient, on the record at the Federal Circuit, to conclude that “enjoining Avadel from applying for FDA approval is necessary to prevent future infringement.” CAFC Op. at 1089. But as explained above, a strong causal nexus exists between the irreparable harm this Court found Jazz will suffer and Avadel requesting approval for IH. Proof of that causal nexus is alone sufficient to enjoin Avadel from requesting approval based on the Court’s initial *eBay* analysis. But as further explained below, Avadel’s request for an IH indication will irreparably harm Jazz.

a. Jazz’s will lose market share to Avadel

Avadel’s request for approval for Lumryz to treat IH will inevitably result in Jazz losing market share to Avadel, a direct competitor, which this Court has acknowledged constitutes irreparable harm. D.I. 665 at 22-24. As explained above, Avadel’s request for FDA approval will necessarily and inevitably result in the sale of Lumryz for IH. *See supra* at 4-15. Because Jazz and Avadel would be “two head-to-head competitors in the [IH] marketplace; every sale of [Avadel’s Lumryz] is a lost sale by [Jazz].” *Sanofi-Aventis Deutschland GmbH v. Glenmark Pharms. Inc.*, 821 F. Supp. 2d 681,694 (D.N.J. 2011), *affd and remanded sub nom. Sanofi-Aventis Deutschland GmbH v. Glenmark Pharms. Inc., USA*, 748 F.3d 1354 (Fed. Cir. 2014).

Xywav IH sales continue to increase at a high rate—a 41% increase from 2023 to 2024. Ex. 18 at 88. But many IH patients have not yet been treated because it is still a nascent market. Thus, Avadel continues to recognize the significant market opportunity. *See supra* at 6-8.

Lumryz’s approval and subsequent prescriptions by healthcare providers would immediately cut Jazz’s market share and irreparably harm Jazz. As previously held, “an encroachment by Avadel at such a ‘crucial inflection point’ in the development of the IH market would harm Jazz by allowing Avadel to ‘capture and define the market with pirated technology.’” D.I. 665 at 23 (citation omitted). “Because Xywav is the only FDA approved treatment for IH, Lumryz’s entrance into the IH market would undoubtedly cause Jazz to suffer significant injury.” *Id.* at 22.

Indeed, Avadel has spent its commercial launch of Lumryz teaching prescribers to switch patients from Jazz products to Lumryz. See D.I. 665 at 3-4. Avadel’s label even includes instructions for prescribers to switch patients from Jazz’s products to Lumryz. Ex. 19 at § 2.4; Bogan Decl. at ¶¶ 21, 36. Avadel’s narcolepsy commercial strategy and labeling instructions teaching prescribers to switch to Lumryz paired with an IH indication will thus inevitably result in prescribers switching patients taking Xywav for IH to Lumryz. Enjoining non-infringing conduct when necessary to prevent infringement is “especially” called for “where, as here, the infringer has taught the market how to infringe or facilitated infringement by end-users” and “the Court cannot trust the infringer not to infringe in the future.” *Global Traffic Techs.*, 2009 WL 10678424 at *8. The Court should prevent the irreparable loss of market share.

b. Jazz will suffer price erosion

Avadel’s request for IH approval will inevitably result in Jazz suffering further price erosion, which this Court held constituted irreparable harm. D.I. 665 at 4-5, 10-12, 23. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] D.I. 665 at 4 (quoting *Sanofi-Synthelabo v. Apotex*,

Inc., 470 F.3d 1368, 1382 (Fed. Cir. 2006)). “[P]rice erosion and loss of market position [i]s likely” if Avadel receives approval for IH. D.I. 655 at 23 (quoting *Purdue Pharma L.P. v. Boehringer Ingelheim GMBH*, 237 F.3d 1359, 1368 (Fed. Cir. 2001)).

Under the injunction, Avadel should not be negotiating with PBMs for additional coverage [REDACTED] due to an additional indication. But Avadel believes that “[o]nce [Avadel] get[s] approval, there should be insurance coverage for LUMRYZ for IH.” D.I. 606, Divis Decl. at ¶ 15. Just as with narcolepsy, this would be to Jazz’s detriment. Once Lumryz is IH-approved, that approval will be public. *See supra* at 12-13. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] The Court should prevent such irreparable price erosion.

c. Jazz will suffer reputational damage

Avadel’s request for IH approval inevitably will result in Jazz suffering irreparable reputational harm. Avadel receiving IH approval will “damage [Jazz’s] ability to build its reputation as the exclusive market leader.” D.I. 665 at 22. This Court found that “Xywav’s title as the only FDA-approved treatment for IH ‘is an intangible asset that is part of a company’s reputation.’” *Id.* at 23 (quoting *Douglas Dynamics, LLC v. Buyers Prods. Co.*, 717 F.3d 1336, 1345 (Fed. Cir. 2013)). Harm to that reputation is irreparable. *Id.* at 23-24.

As explained above, Avadel continues to tout “the potential prospects of LUMRYZ and IH” to investors, clinicians, and key opinion leaders. Ex. 11 at 6; Ex. 16 at 2; Ex. 4 at 4; Ex. 6 at 8:21-24. After approval, Avadel intends to advertise its trial data and IH approval “to the public at large.” No. 24-2274, D.I. 42 at 7, 11 (Fed. Cir. Nov. 13, 2024). Such actions spread the word that Xywav is no longer “the only FDA-approved treatment for IH.” D.I. 665 at 23. The Court should prevent this irreparable reputational harm. This factor still weighs in Jazz’s favor.

2. Monetary remedies will not adequately compensate Jazz

“Jazz has satisfied its burden of showing that monetary remedies would not adequately compensate the harm caused by Lumryz’s introduction into the market for IH.” D.I. 665 at 24. In its original injunction order, this Court found this factor satisfied by evidence of Jazz suffering price erosion, loss of market share to a “head-to-head competitor[],” and reputational harm from losing its exclusivity in the IH market. *Id.* at 22-24 (quoting *Novozymes A/S v. Genencor Int’l, Inc.*, 474 F. Supp. 2d 592, 613 (D. Del. 2007)). As explained above, each of these harms necessarily will result from Avadel’s request for FDA approval for an IH indication for Lumryz. *Natera, Inc. v. ArcherDx, Inc.*, No. 20-125, 2023 WL 9103876, at *4 (D. Del. Dec. 1, 2023) (“[I]nadequacy of remedies available at law[] is nearly indistinguishable from irreparable injury.”). Therefore, this factor still weighs in favor of Jazz’s requested injunction.

3. The balance of equities favors Jazz

“The balance of the equities also tips in Jazz’s favor.” D.I. 665 at 25. Avadel is enjoined from marketing, making, using, or selling Lumryz until the ’782 patent expires. *Id.*; D.I. 733 at 1. Avadel suffers no harm from enjoining an IH approval request until the ’782 patent expires. IH aside, Avadel “expects to generate sustainable positive cash flow in 2025” and make billions from narcolepsy sales alone. Ex. 1 at 5; D.I. 596, 2/27 Tr. (Divis) at 525-527; PTX1899.7.

As explained, Avadel requesting approval for IH will inevitably lead to Avadel marketing and selling Lumryz for IH, which will induce physicians and patients to infringe. *See supra* at 4-15. And the court previously found that “‘requiring [Jazz] to compete against its own patented invention . . . places a substantial hardship on [Jazz],’ particularly given that Lumryz would be the only other FDA-approved treatment for IH.” D.I. 665 at 25 (quoting *Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1156 (Fed. Cir. 2011)) (alterations in original). This factor thus still weighs in favor of Jazz’s requested injunction.

4. The Injunction Would Not Disserve The Public Interest

“In evaluating whether the public interest favors the grant of an injunction, the district court should focus on whether a critical public interest would be injured by the grant of injunctive relief.” *Natera, Inc. v. NeoGenomics Lab ’ys, Inc.*, 106 F.4th 1369, 1380 (Fed. Cir. 2024) (internal quotes and cite omitted). This Court already found “the public interest weighs in favor of enjoining Lumryz in the IH market” because Avadel could not rebut the “public interest in encouraging investment in drug development and protecting the exclusionary rights conveyed in valid pharmaceutical patents[].” D.I. 665 at 25-29 (quoting *Sanofi-Synthelabo*, 470 F.3d at 1383) (internal quotes omitted). Avadel still cannot offer any rebuttal. As explained above, the only way to successfully ensure Lumryz is enjoined from the IH market is to prevent Avadel from requesting approval for an IH indication. Avadel is already enjoined from marketing, making, using, or selling Lumryz for IH. The public is not disserved by this Court “ensur[ing] that the injunctive relief granted is effective.” *Smith & Nephew*, 466 F.Supp.2d at 988.

“[T]he weight of the evidence shows that IH and narcolepsy are distinct conditions and that Xywav can—and very likely is—administered in a single dose to treat the symptoms of IH.” D.I. 665 at 27-28. Avadel “has not [and cannot] show[] that Lumryz offers any other distinct benefits to patients with IH.” *Id.* at 28. This request does not eliminate a choice of drugs, though that alone is insufficient “to disserve the public interest.” *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1381 (Fed Cir. 2017). It simply provides Jazz “such relief that [would be] necessary to make [the current injunction] effective.” *Trans-World*, 750 F.2d at 1564. Therefore, this factor still weighs in favor of enjoining Avadel from requesting approval of Lumryz to treat IH.

IV. CONCLUSION

For the reasons set forth above, Jazz respectfully requests the Court grant the limited permanent injunction requested herein.

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June 17, 2025

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CERTIFICATE OF SERVICE

I hereby certify that on June 17, 2025, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on
June 17, 2025, upon the following in the manner indicated:

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/s/ Jeremy A. Tigan

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EXHIBIT 1

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or Section 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 8, 2025

AVADEL PHARMACEUTICALS PLC
(Exact name of registrant as specified in its charter)

Ireland
(State or other jurisdiction
of incorporation)

001-37977
(Commission
File Number)

98-1341933
(IRS Employer
Identification No.)

10 Earlsfort Terrace
Dublin 2, Ireland, D02 T380
(Address of principal executive offices)

Not Applicable
(Zip Code)

Registrant's telephone number, including area code: **+353 1 901-5201**

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- ☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, nominal value \$0.01 per share	AVDL	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01

Regulation FD Disclosure

On April 8, 2025, Avadel Pharmaceuticals plc issued a press release titled, “Avadel Pharmaceuticals Provides Update at Needham Virtual Healthcare Conference.” A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 7.01, including Exhibit 99.1 hereto, is being furnished herewith and shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01.

Exhibits

(d) Exhibits

[99.1](#) [Press release issued by Avadel Pharmaceuticals plc on April 8, 2025.](#)
104 Cover Page Interactive Data File (embedded with the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

AVADEL PHARMACEUTICALS PLC

Date: April 8, 2025

By: /s/ Jerad G. Seurer

Name: Jerad G. Seurer

Title: General Counsel & Corporate Secretary

Avadel Pharmaceuticals Provides Update at Needham Virtual Healthcare Conference

DUBLIN, IRELAND, April 8, 2025 -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, today presented at the 24th Annual Needham Virtual Healthcare Conference.

The Company provided an update on patient demand metrics that was in line with guidance from its full-year results announcement on March 3, 2025. It also addressed questions related to the recent developments in United States tariff policy and the potential impact on the biopharmaceutical sector, including Avadel.

Specifically:

- In Q1 2025 patient demand metrics for LUMRYZ™, Avadel's innovative narcolepsy medication with a market potential of a billion dollars in peak annual sales, all improved versus Q4 2024. These improvements include patient enrollments, patient starts, persistency rates, and net patients on therapy.
- REVITALYZ™, the Company's Phase 3 pivotal trial studying LUMRYZ in Idiopathic Hypersomnia (IH), is on track to complete enrollment in the second half of 2025.
- Avadel has initiated four patent infringement lawsuits against Jazz Pharmaceuticals since the beginning of 2025, alleging certain uses of Jazz's Xywav product, according to its corresponding labeling, infringe claims of five different Avadel patents.
- The Company expects to generate sustainable positive cash flow in 2025.

Regarding the potential impact of possible changes in U.S. tariff policies, Avadel has developed a diversified supply chain over the past three years for LUMRYZ.

The active pharmaceutical ingredient ("API") in LUMRYZ is sodium oxybate, which is manufactured by two contract development and manufacturing organizations ("CDMOs") located in the U.S. and approved by the U.S. Food and Drug Administration. Accordingly, the U.S. is the country of origin for all the API in LUMRYZ. The finished LUMRYZ commercial product is approved to be manufactured by one outsourced CDMO located in the U.S. and another in Europe. Additionally, all primary packaging of LUMRYZ is conducted in the U.S.

In summary, these efforts have strengthened supply chain security and, if needed, the capability to manufacture LUMRYZ entirely in the U.S.

An archived recording of the fireside chat webcast will be available on Avadel's Investor Relations website, **investors.avadel.com**, for 90 days following the conference.

About LUMRYZ™ (sodium oxybate) for extended-release oral suspension

LUMRYZ is an extended-release sodium oxybate medication approved by the FDA on May 1, 2023, as the first and only once-at-bedtime treatment for cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. On October 16, 2024, LUMRYZ was additionally approved as a once-at-bedtime treatment for cataplexy or EDS in pediatric patients 7 years of age and older with narcolepsy.

The FDA approval of LUMRYZ was supported by results from REST-ON™, a randomized, double-blind, placebo-controlled, pivotal Phase 3 trial in adults with narcolepsy. LUMRYZ demonstrated statistically significant and clinically meaningful improvements in the three co-primary endpoints: EDS (MWT), clinicians' overall assessment of patients' functioning (CGI-I), and cataplexy attacks, for all three evaluated doses when compared to placebo.

With its approvals in May 2023 and October 2024, the FDA also granted 7 years of Orphan Drug Exclusivity to LUMRYZ for the treatment of cataplexy or EDS in adults with narcolepsy and in pediatric patients 7 years of age and older with narcolepsy (respectively) due to a finding of clinical superiority of LUMRYZ relative to currently available oxybate treatments. In particular, the FDA found that LUMRYZ makes a major contribution to patient care over currently available, twice-nightly oxybate products by providing a once-nightly dosing regimen that avoids nocturnal arousal to take a second dose.

About Avadel Pharmaceuticals plc

Avadel Pharmaceuticals plc (Nasdaq: AVDL) is a biopharmaceutical company focused on transforming medicines to transform lives. Our approach includes applying innovative solutions to the development of medications that address the challenges patients face with current treatment options. Avadel's commercial product, LUMRYZ, was approved by the U.S. Food & Drug Administration (FDA) as the first and only once-at-bedtime oxybate for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy. For more information, please visit www.avadel.com

Avadel intends to use its Investor Relations website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company's Investor Relations website, in addition to following the Company's press releases, SEC filings, public conference calls, presentations, and webcast.

IMPORTANT SAFETY INFORMATION

WARNING: Taking LUMRYZ™ (sodium oxybate) with other central nervous system (CNS) depressants, such as medicines used to make you fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope) and death.

The active ingredient of LUMRYZ (sodium oxybate) is a form of gamma hydroxybutyrate (GHB), a controlled substance. Abuse or misuse of illegal GHB alone or with other CNS depressants (drugs that cause changes in alertness or consciousness) have caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma and death. Call your doctor right away if you have any of these serious side effects.

Because of these risks, LUMRYZ is available only by prescription and filled through certified pharmacies in the LUMRYZ REMS. You must be enrolled in the LUMRYZ REMS to receive LUMRYZ. Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

INDICATIONS

LUMRYZ (sodium oxybate) for extended-release oral suspension is a prescription medicine used to treat the following symptoms in patients 7 years and older with narcolepsy:

- sudden onset of weak or paralyzed muscles (cataplexy)
- excessive daytime sleepiness (EDS)

Do not take LUMRYZ if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drink alcohol or have a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep LUMRYZ in a safe place to prevent abuse and misuse. Selling or giving away LUMRYZ may harm others and is against the law. Tell your doctor if you or your child have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Anyone who takes LUMRYZ should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery or flying an airplane, for at least six (6) hours after taking LUMRYZ. Those activities should not be done until you know how LUMRYZ affects you.

Falling asleep quickly, including while standing or while getting up from the bed, has led to falls with injuries that have required some people to be hospitalized.

LUMRYZ can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing and/or short periods of not breathing while sleeping (e.g., sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they take LUMRYZ.

- **Mental health problems**, including confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness and difficulty concentrating. Tell your doctor if you or your child have or had depression or have tried to harm yourself. **Call your doctor right away if you or your child have symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you or your child start sleepwalking.

Tell your doctor if you or your child are on a salt-restricted diet or have high blood pressure, heart failure or kidney problems. LUMRYZ contains a lot of sodium (salt) and may not be right for you.

The most common side effects of LUMRYZ in adults include nausea, dizziness, bedwetting, headache and vomiting. Your side effects may increase when you take higher doses of LUMRYZ. The most common side effects in children include nausea, bedwetting, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking. LUMRYZ can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of LUMRYZ.

For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit <http://www.fda.gov/medwatch>, or call 1-800-FDA-1088.

Please see full Prescribing Information, including BOXED Warning.

Cautionary Disclosure Regarding Forward-Looking Statements

This press release includes “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects or other events. Such forward-looking statements include, but are not limited to, expectations regarding the potential therapeutic benefit of LUMRYZ; the success of the commercialization of LUMRYZ, including the ability to generate positive cash flow; the anticipated market potential and sales opportunity of LUMRYZ; the Company’s idiopathic hypersomnia clinical study for LUMRYZ, including enrollment and timing related thereto; and the Company’s expectations regarding the strength and diversity of its supply chain and the impact of potential tariffs. In some cases, forward-looking statements can be identified by use of words such as “will,” “may,” “could,” “believe,” “expect,” “look forward,” “on track,” “guidance,” “anticipate,” “estimate,” “project,” “next steps” and similar expressions and the negatives thereof (if applicable).

The Company's forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company's business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company's business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company's forward-looking statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of the Company's most recent Annual Report on Form 10-K and subsequent filings with the Securities and Exchange Commission.

Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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EXHIBIT 2

Avadel Pharmaceuticals PLC

Q4 2023 Earnings Call

Mon Mar 04 2024 Earnings Call Transcript

Q4 2023 Earnings Call (Raw version)

Summary NEW

⚡ SMART SUMMARY

Positives • The company generated \$19.5 million net revenue for Q4 2023 and \$28 million of revenue for the seven months ended December 31, 2023. • The company is well positioned to advance LUMRYZ to command a meaningful share of the multi-billion dollar oxybate market and maintains its view that LUMRYZ offers a greater than \$1 billion potential market opportunity. • The company has a healthy balance sheet to support its operations and continued growth. • The company saw an increase in its overall representation of all rights of patients in Q4 compared to Q3. • The company is focused on continuing to have more HCPs by which rise up and the field reimbursement team to get more patients initiated onto LUMRYZ and support them longer term on their LUMRYZ journey.	Negatives • The company saw a \$48 million decrease in cash during Q4, primarily due to net cash used in operations of \$26 million, which is net of cash proceeds from sales of LUMRYZ and \$22 million to pay off the remainder of the convertible notes. • The company is facing challenges in keeping data to themselves.	Outlook • Cash operating expenses before consideration of cash proceeds from sales of LUMRYZ are expected to be in the range of \$40 million to \$45 million per quarter in 2024. • Net cash used for operations is expected to be materially lower after taking into account expected cash receipts from continuing sales of LUMRYZ.

Q & A Highlights • Just - hey, Richard, I think you mentioned over 70% of the top 500 prescribers and I think represent like 50% of the scripts here have prescribed LUMRYZ already. Do you - can you give any granularity as to if they're repeat prescribers, if they've done it with multiple patients, is there a percentage of that or is there kind of a feel of a bullish start? Any color there would be helpful. • A majority of the top 500 oxybate prescribers have been repeat writers of LUMRYZ prescriptions. • Firstly, just with regards to Anthem, what percent of the 00:20:31 GPO volume is Anthem? And maybe for United, what percent of MSR would that comprise? And maybe if you could sort of also comment on just general progress in terms of pull-through at the individual 00:20:51 level across the three different GPOs, that would be helpful to understand. • Anthem is about 30% of the GPO lives and UnitedHealthcare is a similar percentage for the SMR lives. Pull-through is increasing now that there is coverage for lives that meet the prior authorization criteria. • And then, in IH, how are you thinking about that opportunity in terms of your ability to either expand the market ? Or do you think you get a lot of capture from patients who are on the low sodium twice nightly oxybate product? • There is significant opportunity to help more diagnosed IH patients get treated given the low penetration of the current FDA approved drug. LUMRYZ could help patients avoid disruptive middle-of-the-night wakings. • Can you comment on patient types signing up to the RYZUP program and if you see any differentiation than those that ultimately received therapy? Is that a similar process for naïve patients, with discontinued patients and switch patients going through the RYZUP program? • The RYZUP enrollment process is generally the same for naïve, discontinued, and switch patients, initiated by the provider. The amount of information required is generally the same. • So just kind of generally, what are the characteristics of these patients that sit on the program? And, you know, do they not just meet - that did just not meet the PA criteria? And then should we still think of kind of, you know, conversion rate there, you know, reaching very high numbers or some of these patients just sit on the program? • Patients may sit in the RYZUP program for longer if they don't initially meet authorization criteria or aren't a covered life, but the team continues to appeal denials and has seen success getting a large portion of these patients initiated on therapy eventually. • Thanks for taking the questions. I guess maybe can you provide some more color in terms of what you're hearing with respect to how important the low sodium formulation is in the marketplace right now and your strategy there, as you move forward, your formulation? • The field team hears fewer objections about sodium content now. Published data shows no cardiovascular outcome differences between twice nightly sodium oxybate products. Once nightly dosing is also beneficial. The lower sodium formulation will provide an option for patients with sodium sensitivities. • In terms of the IAH 00:42:55 opportunity, you stated that you plan to launch your study the second half of this year. Can you give us more detail in terms of the potential timeline there and of that program? • The IH study will be initiated in the second half of 2023 but it's too early to provide details on enrollment completion. Significant work is underway on trial setup and the team will provide more updates as progress continues.

Event Details

Date: 2024-03-04
Company: Avadel Pharmaceuticals Plc
Ticker: AVDL-US

Company Participants

Austin Murtagh - Stern Investor Relations, Associate Director
Gregory J. Divis - Avadel Pharmaceuticals Plc, Chief Executive Officer & Director
Richard Kim - Avadel Pharmaceuticals Plc, Chief Commercial Officer
Thomas S. McHugh - Avadel Pharmaceuticals Plc, Chief Financial Officer
Unverified Participant

Other Participants

François Brisebois - Analyst
Ami Fadia - Analyst
Andrew Tsai - Analyst
David Amsellem - Analyst

Chase Knickerbocker - Analyst

Rudy Li - Analyst

Matt L. Kaplan - Analyst

Oren Livnat - Analyst

MANAGEMENT DISCUSSION SECTION

Operator

00:00:03 Greetings and welcome to Avadel Pharmaceuticals Fourth Quarter and Full-Year 2023 Earnings Call. At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation. As a reminder, this conference is being recorded.

00:00:23 It is now my pleasure to introduce Austin Murtagh with Stern Investor Relations. You may begin.

Austin Murtagh

00:00:31 Good morning, and thank you for joining us on our conference call to discuss Avadel's fourth quarter and full-year 2023 earnings. As a reminder before we begin, the following presentation includes several matters that constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. This includes statements related to expectations regarding revenue, operating expenses, and operating breakeven. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those contemplated in such forward-looking statements.

00:01:08 These risks and uncertainties are described in Avadel's public filings under the Exchange Act included in the Form 10-K for the year ended December 31, 2023, which was filed on February 29, 2024, and subsequent SEC filings. Except as required by law, Avadel undertakes no obligation to update or revise any forward-looking statements contained in this presentation to reflect new information, future events or otherwise. For purposes of this conference call, the company made the decision to provide certain leading launch indicators as of January 31, 2024, in order to provide a more current snapshot of its launch progress and in consideration of the update the company provided in early January. Avadel undertakes no obligation to provide intra-quarter results in future quarters.

00:02:02 On the call today are Greg Divis, Chief Executive Officer; Richard Kim, Chief Commercial Officer; and Tom McHugh, Chief Financial Officer.

00:02:11 At this time, I'll turn the call over to Greg.

Gregory J. Divis

00:02:15 Thank you, Austin. Good morning, everyone, and thank you for joining us for a company update and to review Avadel's fourth quarter and full year 2023 results.

00:02:25 Following my brief opening remarks, Richard will provide an update on our launch progress, including our key metrics through January 31. Tom will then review our Q4 financial results and provide some commentary regarding 2024. We will conclude with a question-and-answer session.

00:02:41 As most of you are likely aware, it's been a busy several days for Avadel, especially last week with the ongoing patent trial in Delaware, where closing arguments were heard this past Friday. And we are now awaiting a jury's decision.

- 00:02:54 So before we dive into the commercial and business updates announced in our press release this morning, I would like to take a moment to provide some general commentary as it relates to the current and still active patent dispute. Regardless of the outcome, we own it – we don't expect the pending jury decision in the patent trial to impact our ongoing commercial launch or our belief in the potential LUMRYZ.
- 00:03:19 Given this is an active litigation, we will not provide any further commentary or answer any questions on the trial, the underlying dispute or the pending decision at this time. However, as we have it, all key matters. We will provide an update when the trial concludes, and we appreciate your understanding on this point.
- 00:03:39 2023 was truly a monumental year for Avadel with final FDA approval, we were able to bring LUMRYZ to the narcolepsy community and execute our initial launch plan, both of which have been transformational for the company and that we have worked towards for many years.
- 00:03:54 In addition to the unmatched achievement of launching LUMRYZ within approximately one month of final FDA approval, since launch last June, LUMRYZ has seen strong uptake among patients and prescribers, which has been supported by the positive feedback we've received from the broader narcolepsy community.
- 00:04:11 Our early loss momentum throughout 2023 has continued into this year as demonstrated by progress being made across physicians, patients, and payers, all of which Richard will provide further details on shortly. Our team's nearly decade-long dedication to advancing LUMRYZ into the sleep medicine space overall has allowed us to build a foundation for continued growth and the potential expansion of LUMRYZ.
- 00:04:35 And as such, our priorities as a company remain very crystal clear. First and foremost, continues to be our focus on executing our launch strategy and delivering on the promise and the potential of LUMRYZ across the multibillion-dollar oxybate market opportunity. We are proud of the momentum we are building and all we have accomplished thus far. And this is evidenced by the \$19.5 million in LUMRYZ net revenue in the fourth quarter and the \$28 million for the seven months ended December 31, 2023.
- 00:05:04 Our second and near-term opportunity is our potential expansion into the pediatric narcolepsy population. The FDA accepted our supplemental new drug application for LUMRYZ for the treatment of cataplexy or excessive daytime sleepiness in patients between the ages of 7 to 17 with narcolepsy and provided us an action date of September 7, 2024. We believe approval in the pediatric population will allow LUMRYZ to provide further positive impact to the narcolepsy community and caregivers at large.
- 00:05:37 We have heard directly from parents about the challenges associated with the middle-of-the-night dosing and the burden a twice-nightly dosing regimen may create for the entire family. We believe LUMRYZ, if approved, for the pediatric population, can offer the potential of reducing that treatment burden while also providing an effective treatment for children living with narcolepsy.
- 00:05:58 We look forward to the potential approval and launch later this year.
- 00:06:03 The next growth opportunity we're pursuing is LUMRYZ for the treatment of idiopathic hypersomnia or IH. When speaking with key opinion leaders in the field, there is a significant need for the use of once-at-bedtime LUMRYZ for many suffering from the deep sleep inertia associated with IH. With a current estimated uniquely diagnosed IH patient population of greater than 30,000, we believe LUMRYZ, if approved for the IH indication, will be an important addition to the treatment options for those suffering from this rare sleep disorder, while also providing potentially meaningful upside to the future value of LUMRYZ.
- 00:06:42 We are currently well advanced in the planning stages to initiate a multicenter, randomized controlled trial for IH in the second half of this calendar year. And we intend to provide updates as we reach various important milestones, including when our first patient is enrolled. And lastly, we're continuing the pre-clinical development work of a potential no or low-sodium once-at-bedtime oxybate formulation with a target product profile that is bioequivalent to LUMRYZ. And we intend to provide those updates as appropriate as well.
- 00:07:15

In closing, we ended this year in a strong position with a healthy balance sheet to support our operations and our continued growth. Coupled with the progress already made this year, we believe we are well positioned to expand our reach and impact within the sleep medicine space and, most importantly, continue executing the launch of LUMRYZ.

00:07:34 I am proud of the significant accomplishments and progress our team has delivered over the past year and remain highly confident that we will continue that during the year ahead. We believe we are well positioned to advance LUMRYZ to command a meaningful share of the multi-billion dollar oxybate market and maintain our view that LUMRYZ offers a greater than \$1 billion potential market opportunity.

00:07:57 With that, I'll turn the call over to Richard for details on our commercial progress. Richard?

Richard Kim

00:08:02 Hey, thanks, Frank and good morning, everyone. I'm excited to share our launch progress and provide some insight into the trends we find develop as we enter 2023 and early into this year. Now taking a step back and looking at what we achieved this past year. We are so proud to be part of a team that has been able to bring a life changing treatment to the narcolepsy community.

00:08:23 The positive feedback we hear from both people with narcolepsy and healthcare providers every day continues to be an inspiration for us. Great touch on this earlier, but our luminous commercial results continue to be strong since we launched last June, and we remain laser focused on keeping the momentum growing in 2024.

00:08:43 Starting with patients RYZUP enrollments are an important indicator of early launch demand, as it is really the first step in the process for patients to receive their LUMRYZ prescription. We previously stated that as of December 31, there were over 1,900 patients enrolled RYZUP. Since that time, we've continued this strong demand with now greater than 2,200 patient enrollment through the end of January.

00:09:11 Turning to patients who have initiated therapy. As of December 31, there were a 1,000 patients who had initiated LUMRYZ treatment and that number grew to greater than 1,200 by the end of January. Typically the start of the year can be more complicated to initiate new therapies. So we were pleased to see that we did not lose any momentum in getting LUMRYZ patients started.

00:09:33 Importantly, the majority of these patients are commercially reimbursed. When we look at our available RYZUP data, we can view see all three patient segments, switch patients from first generation oxybate patients who previously tried and discontinued or first generation oxybate and An oxybate naïve patients being well represented. We are seeing the majority of initiations come from patients switching from a first generation oxybate with more patients coming from the twice nightly mix salts product compared to the twice nightly sodium oxybate product.

00:10:06 For new to oxybate patients, we saw an increase in our overall representation of all rights of patients in Q4 compared to Q3. We're also excited that in the next few weeks we will be rolling out our album LUMRYZ ambassador program, where people with narcolepsy will begin to tell their stories of how LUMRYZ has transformed their lives. These stories and messages will come out through various forms of media to get these personal messages about LUMRYZ out to the narcolepsy community.

00:10:34 Turning to health care providers. As of January 31, there were approximately 1,900 HCP who are REM certified. As previously stated, although we cover the 4,500 plus HCP who make up the entire oxybate prescribing universe, we have been spending more time with the 1,600 high volume prescribers who make up 80% of the total oxybate market.

00:10:58 Of these prescribers, we have focused more of our early efforts on the almost 500 most experienced prescribers who account for 50% of the overall oxybate market and greater than 70% of these top tier HCPs have now written a prescription for LUMRYZ. Every week we have been consistently adding more new and repeat writers. Additionally, in the fourth quarter, we began our KOL and speaker programs as a key tactic to drive HCP peer-to-peer LUMRYZ education.

- 00:11:26 For product fulfillment, we continue to make strong progress demonstrated by the greater than 1,200 patients who have initiated therapy as of January 31. As our overall reimbursement has grown significantly, we are focused on continuing to have more HCPs by which rise up and our field reimbursement team to get more patients initiated onto LUMRYZ and support them longer term on their LUMRYZ journey.
- 00:11:51 In February, we saw continued improvement and progress with our trends.
- 00:11:56 That's a nice segue way for me to provide an update on our payer progress. We announced that with the signing of Emisar contract, we secured all three GPO contracts last year within the first seven months of launch. Now, to start 2024, LUMRYZ is now also covered by Anthem and the UnitedHealthcare national formulary. LUMRYZ now has coverage policies with greater than 80% of commercially covered lives or over 140 million lives. With the recent payer wins in hand, positive feedback from 00:12:27 and people with narcolepsy, growing momentum in product fulfillment, and strong execution from our team, we believe we are well-positioned for long-term LUMRYZ growth and ultimately for LUMRYZ to become the preferred oxybate for people with narcolepsy and HCP.
- 00:12:45 With that, I look forward to providing more updates on future calls. And, now, I will turn the call over to Tom to discuss our financials. Tom?

Thomas S. McHugh

- 00:12:54 Thank you, Richard. Before we begin, I'll note the full financial results are available in the press release issued this morning and the 10-K that was filed last week. We are pleased to report that we generated \$19.5 million net revenue for the quarter ended December 31, 2023, and \$28 million of revenue for the seven months ended December 31, 2023. And as of December 31, we estimate that there was approximately one month of demand in the channel.
- 00:13:22 Turning to operating expenses, we reported \$43.7 million of total GAAP operating expenses for the fourth quarter 2023 compared to \$28.3 million in the fourth quarter of 2022. Total operating expenses in the fourth quarter of 2023 includes \$4.6 million of noncash charges comprised of stock-based compensation of \$3.5 million and depreciation and amortization of \$1.1 million.
- 00:13:47 compensation of \$3.5 million and depreciation and amortization of \$1.1 million. After adjusting for these items, cash operating expenses were approximately \$39 million for the quarter. For the full year of 2023, GAAP operating expenses were \$165 million compared to \$98.6 million in 2022. Excluding stock-based compensation of \$15.8 million and depreciation and amortization of \$4.3 million, cash operating expenses for the full year of 2023 were approximately \$145 million.
- 00:14:22 The increase in year-over-year operating expenses for both the fourth quarter and full year is primarily attributable to loss-related costs, higher compensation costs related to increased head count and legal costs. These were offset by lower R&D costs. Prior to FDA approval on May 1, 2023, inventory expenses, inventory purchases were expensed as R&D.
- 00:14:52 With respect to the balance sheet, as of December 31, we had \$105 million of cash, cash equivalents and marketable securities compared to \$153 million on September 30, 2023. The \$48 million decrease in cash during the fourth quarter is primarily due to net cash used in operations of \$26 million, which is net of cash proceeds from sales of LUMRYZ and \$22 million to pay off the remainder of the convertible notes. As a result of paying off the notes, we are now effectively debt free.
- 00:15:23 During 2024, we currently expect that cash operating expenses before consideration of cash proceeds from sales of LUMRYZ will be in the range of \$40 million to \$45 million per quarter. We believe that net cash used for operations will be materially lower after taking into account expected cash receipts from continuing sales of LUMRYZ.

00:15:48

As we look ahead based on current trends, plans and assumptions, we believe we can achieve operating breakeven when there are approximately 1,300 to 1,500 commercially reimbursed patients on therapy and that we can achieve this during 2024. In addition to the number of reimbursed patients on therapy, our expectations regarding breakeven take into account a number of other assumptions, including how quickly patient demand grows, net pricing of LUMRYZ and operating expenses to support the launch of LUMRYZ.

00:16:18 Now, I'll wrap up with some commentary regarding 2024 revenue. While we are not providing formal guidance at this point, we pay close attention to the sell side estimates. And at this time, we are comfortable with the current consensus of approximately \$155 million for the full year, including the possibility that 2024 revenue could be higher if actual results for LUMRYZ, such as the rate of increase in commercially reimbursed patients, the total number of reimbursed patients who are treated with LUMRYZ, and net pricing outperform the assumptions currently used by the sell side.

00:16:55 And with that, I will turn the call back to Greg for closing remarks.

Gregory J. Divis

00:16:59 Thank you, Tom. With the strong foundation our team has built and the tenacity in bringing LUMRYZ to the narcolepsy community, we are pleased to see the momentum we created last year has continued as we've entered 2024. Our 2024 priorities are clear, and we remain intently focused on our launch execution while bridging to cash flow breakeven and the near-term expansion opportunities for Avadel with our lifecycle management strategy.

00:17:32 We thank you for your support. We look forward to providing future updates on our progress. And with that, we will open the call for questions. Operator?

QUESTION AND ANSWER SECTION

Operator

00:17:45 Thank you. We do ask that you limit to one question and one follow up. Please stand by while we compile the Q&A roster. The first question comes from François Brisebois with Oppenheimer. Your line is open.

Analyst: François Brisebois

00:18:01 **Question – François Brisebois:** Hi. Thanks for taking the question. Just – hey, Richard, I think you mentioned over 70% of the top 500 prescribers and I think represent like 50% of the scripts here have prescribed LUMRYZ already. Do you – can you give any granularity as to if they're repeat prescribers, if they've done it with multiple patients, is there a percentage of that or is there kind of a feel of a bullish start? Any color there would be helpful.

00:18:29 **Answer – Unidentified speaker:** Yeah. Hey, François. Good morning and thanks for the question. Yeah. You know, I think overall, if we think about those top 500, they are the largest volume oxybate prescribers. We've very pleased to sort of see that penetration that we've had. And a majority of those folks have been repeat writers as well.

00:18:45 You know, some of them have adopted it at different times along their journey here. But we have, like I said, broken over 30% with the vast majority of those being repeat writers at this time as well.

00:18:55 **Question – François Brisebois:** Okay. Great. And then in terms of the – you know, I don't know if – is reimbursement have an impact on how quickly someone gets the product in their – a patient gets the product in hand. Is that evolving with time or any color there at all would be helpful. Thank you.

00:19:15 **Answer – Unidentified speaker:** Yeah. Yeah. And Greg, so do you want me to take that one?

00:19:18 **Answer – Unidentified speaker:** Yeah, go ahead, Richard.

00:19:20 **Answer – Unidentified speaker:** Yeah, sure. Thanks again, François. So, yeah, as far as reimbursement is concerned, yeah, it does matter. Actually, for us, what we generally see is if patients are covered and they meet the prior authorization criteria, it's not only, you know, we sort of a given guideline for about a month, but it's definitely been creeping under a month if you have coverage and you meet the criteria.

00:19:40 So that coverage does matter for us quite a bit here, and we're seeing more of those patients now going through under that period where they do actually have coverage and they meet the criteria. So, those patients are now going through in well under a month period of time.

Unidentified speaker

00:19:56 **Question – Unidentified speaker:** Okay. Great. Thank you and congrats on the quarter, guys.

Answer – Unidentified speaker: Thanks, 00:19:59.

Operator

00:20:11 The next question comes from Ami Fadia with Needham. Your line is open.

Analyst:Ami Fadia

00:20:18 **Question – Ami Fadia:** Good morning. Thanks for taking my question and congrats on all the progress that you've made. Maybe two questions for me. Firstly, just with regards to Anthem, what percent of the 00:20:31 GPO volume is Anthem? And maybe for United, what percent of MSR would that comprise? And maybe if you could sort of also comment on just general progress in terms of pull-through at the individual 00:20:51 level across the three different GPOs, that would be helpful to understand.

00:20:57 And maybe my second question is, what are you doing to sort of continue to drive this growth at the top of the funnel in terms of adding more patients to rise up? And what are sort of some of the objectives for 2024 with that regard? Thank you.

00:21:16 **Answer – Unidentified speaker:** Richard, you want to take those?

00:21:17 **Answer – Unidentified speaker:** Yeah, sure. Thanks, Ami, for the questions. Yeah. So, yeah, first, we're super excited that we have those coverage decisions with both Anthem and UnitedHealthcare, to your point, pushing out over 80% commercially covered lives. Anthem and UHC are both pretty big for their respective GPOs. Anthem, probably in the neighborhood of about 30% of the lives and UnitedHealthcare probably less similar for the SMR lives as well. So, pretty significant large plans where we now have that coverage as well.

00:21:40 As far as the pull-through is concerned, sort of as per the previous question, we're definitely seeing now where there is a covered live and patients meet the prior authorization criteria, which is somewhere to 00:21:57, you know, most other oxybates that those lives are being pulled through those prescriptions are being pulled through quicker now as well.

00:22:05 So the coverage does matter for us, and we're seeing that pull-through starting to increase our overall conversion rate across the team here as well.

00:22:14 Now to your last question as far as growth drivers for demand, we see several still. When it comes to the ACPs, you know, as we talked about before, there are ACPs who adopt at various stages along the

adoption curve. We began our speaker programs to have peer to peer education going on for those physicians going forward from that fourth quarter of last year.

00:22:37 I also just announced earlier that our larger patient initiatives will be given in the next few weeks through our brand ambassadors for LUMRYZ where they will share their stories about what LUMRYZ has done for them. And we plan to get those out through various forms of media as well. So it's really a two-pronged approach, which is to continue our efforts against ACPs and to also elevate the voice within the patient community as well.

Unidentified speaker

00:23:03 **Question – Unidentified speaker:** Got it. Thank you.

Operator

00:23:06 One moment for the next question. The next question comes from Andrew Tsai with Jefferies. Your line is open.

Analyst:Andrew Tsai

00:23:17 **Question – Andrew Tsai:** Hey. Good morning. Congrats on the strong execution and thanks for taking our question. So the first one is around, you know, conversion rates and discontinuation rates. 2,200 patients have cumulatively 00:23:32 signed up. It's a great number. You've confirmed break even for this year.

00:23:35 breakeven for this year. So, is it still fair to assume that most or at the large majority of these signups are bound to convert, suggesting discontinuation rates should still remain very favorable and may be directionally well below 25%?

00:23:52 And secondly, you're on a great trajectory, you know, with the strong monthly ads, the healthy conversion rates, again, your blessing 2024 results like consensus number. So obviously, the trajectory cannot last forever. So when should the street start to consider or model a change in the slope? Thank you.

00:24:14 **Answer – Unidentified speaker:** Richard, do you want to maybe take the first the conversion and discontinuation rate?

00:24:18 **Answer – Richard Kim:** Sure. I'll take those. And thanks for the question, Andrew. Yeah. So, yeah, we're very pleased with what the team has been doing through RYZUP 00:24:26 reimbursement team for conversion. We are seeing our overall conversion rate start to increase over time here as well. So and, you know, we're seeing both an improvement in the time, especially with patients who are covered with, who meet the TI criteria. But at the same time, we're not giving up on some of the enrollments that have been in our system for a longer period of time. Sometimes they just require a little bit more work.

00:24:50 But along with that to your point, our discontinuation rate is below what we've seen historically for the twice monthly oxybate. I think I've referenced 25%, which is about the benchmark of discontinuation for twice nightly at one month. So we are seeing our rate of discontinuation rate below the historical, quite frankly, claims historically.

00:25:09 So to your point, we see a sort of a nice build up getting more new patients on. And currently, we have a lot of efforts to appropriately keep patients on persistently over time as well. Greg, I'll maybe pass the last question over back to you.

00:25:22 **Answer – Gregory J. Divis:** Yeah. Just a couple of comments. First, I think when it relates to conversions and discontinuation rates, I think, you know, with two full quarters into the launch, I think we've done incredibly well in both conversion to initiating on therapy and how we've effectively manage the

discontinuation rates I think we've done incredibly well in both conversion to initiating on therapy and how we've effectively manage the discontinuation rates through all of our programs and services. So Richard's right, we're really pleased where we sit and certainly we believe are beating the benchmark relative to the existing therapies in the marketplace.

00:25:49 As it relates to your comment about, you know, when should we guide the street to, you know, change an expectation around the slope of the curve, right, listen, we're not going to guide specifically around that, Andrew. I appreciate the question, but I'll just remind everyone that, like there is a large number of patients who have – who are in our oxybate market opportunity. That's upwards of 50,000 potential patients when you take in the currently existing treated patients across all forms of 00:26:19 oxybate previously discontinued and new starts. We certainly expect to see us to continue to drive demand from those – all sources of those patients at this point in time. So, you know, there's a large pie out there. And, you know, our view is that, you know, we haven't – we haven't hit the flattening of our slope at this point.

Unidentified speaker

00:26:42 **Question – Unidentified speaker:** Great. Thanks again and looking forward to seeing more good news.

Operator

00:26:48 One moment for the next question. The next question comes from David Amsellem with Piper Sandler. Your line is open.

Analyst:David Amsellem

00:27:01 **Question – David Amsellem:** Hey. Thanks. So, on the pediatric opportunity, can you talk about realistically how many patients you could capture or percentage of the market you think you can capture with a once nightly modality?

00:27:18 So, that's number one. And then, in IH, how are you thinking about that opportunity in terms of your ability to either expand the market ? Or do you think you get a lot of capture from patients who are on the low sodium twice nightly oxybate product?

00:27:38 Just how you're thinking about those commercial dynamics in NIH. Thank you.

00:27:42 **Answer – Unidentified speaker:** Yeah. Thanks, David. On pediatrics, you know, depending upon your data source, you know, and there's different, you know, if you will, claims data sources, we would – it would tell us that the actual oxybate utilization of pediatric patients relative to the total pie is anywhere from 3% to 5%. So it's a relatively small patient population in the context of the full pie.

00:28:07 And part of that is because although onset of symptoms occurs between the ages, normally between the ages of 7 and 17, the diagnosis, actually, the proper diagnosis doesn't occur to somewhere between 8 to 15 years later, which is something that, you know, certainly everyone hopes improves over time. So for us, it really has been it's much less about, you know, the total patient population that are pediatrics who are being treated and much more about, you know, really meeting the needs of that patient population and their family, right.

00:28:42 We've heard extensively from them about how disruptive waking up in the middle of the night is for parents, for the children and for their families. And so for us, it's a really straightforward opportunity for us to advance to this patient segment and seek approval for it. Again, so we do think there's an opportunity to potentially expand that treated patient pool at this stage. But it's much more about just serving a community within the total narcolepsy patient community who really is looking for the opportunity to not wake up.

00:29:17 With regards to IH, you know, again, with over 30,000 uniquely diagnosed patients and upwards of another greater than 10,000 to 12000 patients who we would describe as diagnosed with IH and narcolepsy And

then you look at there's only one FDA approved drug and you look at, you know, the penetration in that diagnosed patient population at under 10%. We think there is a significant opportunity in IH to help more patients that are being treated.

00:29:50 And again, when we hear from key opinion leaders and physicians at large, the first two things we hear from them after we talk about LUMRYZ narcolepsy, is when are you going to get pediatrics and when are you going to get IH? When are you going to study an IH? And for IH it really is about the fact that these patients suffer from really deep sleep inertia to the extent where they're sleeping, you know, 14, 15, 16 plus hours a day.

00:30:16 And it's hard for them to wake up, right? It's hard for them to wake up. And the opportunity to not be forced to do that in the middle of the night just offers a value proposition. That is, you know, that I would say the community is very interested in with LUMRYZ. So we're excited to initiate that study and, and update everyone on as we progress it and and try to help those patients as well. And we think it's a it's another meaningful upside for the long-term value of LUMRYZ for sure.

00:30:44 **Answer – Unidentified speaker:** Okay. Thanks, Greg.

00:30:45 **Answer – Unidentified speaker:** David.

Operator

00:30:47 One moment for the next question. The next question comes from Ash Verma with UBS. Your line is open.

Unidentified speaker

00:30:58 **Question – Unidentified speaker:** Thanks. Good morning. Congrats from my side as well. So had two questions in terms the switch patients. Can you provide some color on how much of the users coming from REM versus IV a lot of us were surprised to see that 00:31:12 narcolepsy patients are starting to flatten out in the most recent quarter. And then secondly, if you can 00:31:20 you mentioned if you're seeing any off label use on the IH side. Thanks.

00:31:28 **Answer – Unidentified speaker:** Richard, do you want to?

00:31:29 **Answer – Unidentified speaker:** Yeah. No problem. Thanks for the questions, Ash. So yeah, as far as the switch patients are concerned, we do see more coming from the mixed salt 00:31:37 than we do from the twice of the sodium oxybate segment overall as well. You know, just a couple perspectives here, when we did market research early on in the 00:31:49 launch, we saw that a lot of patients there tended to be earlier adopters of newer therapies and maybe we're seeing some of this here as well. There are there are some there are more patients in the marketplace in the mixed salt version right now as well.

00:32:01 But fundamentally, what we also hear is the amount of wet salts that are associated with GHB really had no impact on the narcolepsy outcome. So it's really not much surprise to us that we're seeing more patients switching from the twice from the mixed salt version than the twice-nightly sodium oxybate versions as well. And, you know, to answer your, your question about off-label usage, you know, clearly, first and foremost, we don't we don't promote any off-lable usage, but we have seen requests for off-label use for like pediatrics and for 00:32:35 patients as well.

Unidentified speaker

00:32:40 **Question – Unidentified speaker:** Thank you.

00:32:41 **Answer – Unidentified speaker:** Thanks, Ash.

Operator

00:32:41 One moment for the next question. The next question comes from 00:32:48 with LifeSci Capital. Your line is open.

Unidentified speaker

00:32:54 **Question – Unidentified speaker:** Thank you. Good morning. Just some quick question for me. Can you comment on patient types signing up to the RYZUP program and if you see any differentiation than those that ultimately received therapy? Is that a similar process for naïve patients, with discontinued patients and switch patients going through the RYZUP program?

00:33:14 **Answer – Unidentified speaker:** Richard. Do you want to take that?

00:33:16 **Answer – Unidentified speaker:** Yeah, sure. Thanks, Marian. So, yeah, yeah, the process is quite similar because, like, you know, the way I described the RYZUP enrollment, it's almost like a prescription and the only reason it isn't is because we have three different specialty pharmacies within our network. So, the process is generally initiated by the provider. And the amount of information that's required, depending on what type of patient you are, is generally the same if you are a switch with the exception of 00:33:42, which indicates if you had former usage of an oxybate. So, yeah, we tended to be generally consistent across the board there as well, and we're clearly very pleased to sort of see strong demand coming into RYZUP as well.

Unidentified speaker

00:33:58 **Question – Unidentified speaker:** Okay. Got it. And then you spoke of KOL 00:34:01 speaker program today. Can you provide a bit more detail on what that entails?

00:34:05 **Answer – Unidentified speaker:** Yeah. We – one of the things that's very important, if you think about it, beyond the terrific work that our medical team has done with publications and presentations at scientific medical congresses, it's pretty much been our voice carrying the word for LUMRYZ. So, we now have a speaker bureau. We have trained experts in narcolepsy across the country who are now doing speaker programs on our behalf. We're generally speaking to other providers and some of their colleagues with 00:34:37. And it's been really great to sort of see, we did quite a few of these programs as we exited Q4 of last year. We have executed many more of those programs in Q1 of this year. And we're also doing things such as like national programs. There's broadcast programs as well.

00:34:52 So, it's really a great opportunity to get a fair and balanced sort of perspective out on LUMRYZ in the narcolepsy marketplace. And the reception and the trend has been really positive 00:35:01 that many sort of 00:35:04 specials that have come out of this program. So, getting that peer-to-peer indication out for 00:35:08, we think, is quite critical, and these speaker programs are a very important tactic for us to execute that.

Unidentified speaker

00:35:16 **Question – Unidentified speaker:** Okay. Got it. Congrats on the great year.

00:35:19 **Answer – Unidentified speaker:** Thank you.

Operator

00:35:20 One moment for the next question. Our next question is from Chase Knickerbocker with Craig-Hallum.

00:35:28 Your line is open.

Analyst:Chase Knickerbocker

00:35:32 **Question – Chase Knickerbocker:** Good morning, guys. Yeah, great update. I share my congrats as well. So I just want to maybe better characterize, you know, those patients that sit in the RYZUP program for longer. You know, in some instances it looks like much longer than the one month average you kind of mentioned. So just kind of generally, what are the characteristics of these patients that sit on the program? And, you know, do they not just meet – that did just not meet the PA criteria? And then should we still think of kind of, you know, conversion rate there, you know, reaching very high numbers or some of these patients just sit on the program? Thanks.

00:36:06 **Answer – Unidentified speaker:** Richard, do you want to take that?

00:36:07 **Answer – Unidentified speaker:** Yeah, sure. Thanks, Chase. Yeah. So it's a great observation as far as some of these patients who have been in the process for longer. You know, to your point, the general characterization is they may not have met the authorization criteria or in some cases they weren't covered live.

00:36:23 You know what -what we first seen with the process is then if it's a medical necessity or it's going through an appeal and then a denial process. Now, one of the things we're very proud of, what we've built with the RYZUP team, as well as the tenacity of the team there to not give up on these cases.

00:36:39 So while on one hand, we're very focused on sort of faster turnaround time, especially for patients who need all the criteria. To your point, we're also not giving up on these longer standing cases. So in generally what we have seen as a pretty good success rate, oftentimes after many rounds of appeals and denials going through where we still can get a large portion of these patients initiated on to reimburse therapy as well.

00:37:02 And so – and to that point where we see some time enrollments that started back six months ago, who can ultimately get on the therapy as well. So it's still relatively early to sort of us for us to figure out what those success rates should look like. But we are still seeing on a monthly basis sort of what we would call more aged RYZUP cases who are successfully able to enter therapy, sometimes several months later.

00:37:19 We're successfully able because we have the therapy as sometimes several months later.

Unidentified speaker

00:37:28 **Question – Unidentified speaker:** Makes sense, Richard. Thank you.

00:37:29 **Answer – Unidentified speaker:** Sure. No problem. Thanks, Chase.

Operator

00:37:32 One moment for the next question. Next question comes from Marc Goodman with Leerink. Your line is open.

Analyst:Rudy Li

00:37:45 **Question – Rudy Li:** Thanks for taking my question. This is Rudy on the line for Marc. Congrats on the strong results. So I have question regarding the market dynamics to see the total 00:37:55 market continue to expand in the coming years. And also curious about your thoughts on the opportunity to oxybate products and to see any potential impacting Oxybate in NT1 versus NT2 NIH. Thanks.

00:38:14 **Answer – Unidentified speaker:** Thanks, Rudy. Richard, do you want to take that as well?

00:38:17 **Answer – Unidentified speaker:** Yeah, no. Thanks, Rudy. Yes, so as far as the market dynamics is concerned, yeah, you know, prior to launch, we had done six different quad market research studies that really showed with the introduction LUMRYZ that the Oxybate market could expand with the new patients start somewhere in the neighborhood of 30% to 50%.

00:38:36 It's hard for us to sort of say right now because some of the other data from other companies is no longer as visible as it used to be. So, you know, we're – but what we're definitely seeing right now is a few things. One is we're getting more people who had never prescribed oxybate previously into the mix who prescribe. And we're seeing, you know, obviously strong penetration within existing oxybate prescribers. So, we definitely believe we're sort of seeing some of the dynamics of patients going beyond using LUMRYZ where they maybe were more limited with twice on the oxybate.

00:39:10 And as far as I think your question around, 00:39:12 are concerned. You know, for us, we're very excited to see any new treatment modalities that could potentially come to the marketplace. Obviously, those companies still have to go through the clinical and regulatory process as well.

00:39:25 The first one that we start to see is focusing more on NT1. You know, I guess a couple of things that we sort of see when it comes to erections. They like to be really fabulous weight promoting agents, maybe a little less often around their impact on sleep. And clearly, there's a lot of questions around the overall benefit risk profile between efficacy and tolerability as well.

00:39:46 But the one thing we do know overall is this tends to be a polypharmacy marketplace. It has been in the past and it likely will be in the future as well. So we believe that we might as well positioned, you know, not only in NT2, but really because of the benefit that it has in NT1 as well. So I think we're still early on there as well. But you know, one thing that we always consider oxybates are used today in about less than 10% of patients who are diagnosed and under care for narcolepsy. You know, so we still see there's lots of room for our space to grow, as Greg had mentioned previously. And we believe we're well positioned today and also as new therapies come out in the future as well.

Unidentified speaker

Question – Unidentified speaker: Thanks.

00:40:31 **Answer – Unidentified speaker:** Thanks, Rudy.

Operator

00:40:31 One moment for the next question. Next question comes from Matt Kaplan with Ladenburg Thalmann. Your line is open.

Analyst: Matt L. Kaplan

00:40:44 **Question – Matt L. Kaplan:** Hey. Good morning, guys. Thanks for taking the questions. I guess maybe can you provide some more color in terms of what you're hearing with respect to how important the low sodium formulation is in the marketplace right now and your strategy there, as you move forward, your formulation?

00:41:03 **Answer – Unidentified speaker:** Richard, do you want to talk about that?

00:41:07 **Answer – Unidentified speaker:** Yeah. I think the first part there, Matt. Thanks. So, yeah. You know, candidly, you know, from our field, we hear a lot less objections about sort of sodium content overall. I'd say

a couple of things. First, you know, there's – we now have sort of you know, there is – we now have sort of our team out there as well.

00:41:21 Secondly, one of the key publications that our team uses is a publication that came out in 2020, where sleep experts from Stanford and UCLA looked at the sort of the history of twice nightly sodium oxybate and their conclusion was that there was really no difference in cardiovascular outcomes on patients on twice nightly sodium oxybate products at that time. So I think 00:41:44 what's happened is science is sort of being focused on here and there's good published data that's able to be used. And it's also – there's another copy out there talking about the benefits of what a once bedtime therapy can do overall. So we really haven't heard as much of that in the field is 00:42:04 ACPs focusing on that. But I think now that patients – or ACPs are getting experience with LUMRYZ and seeing the benefit of what it can offer to their patients, I think that's held a lot of weight with 00:42:15 as well. And I don't know, Greg, if you want to talk about our lower sodium as well?

00:42:20 **Answer – Unidentified speaker:** Yeah. I think in that regard, Matt, I think our view is, is that there are patients who have sodium sensitivities or other comorbidities that may require them to accommodate for that in their oxybate treatment choice. And we want to make sure all those patients have an opportunity to be on a once-at-bedtime therapy option. So that's why we continue to proceed with it. And from that perspective, we think everyone should have that option.

Unidentified speaker

00:42:51 **Question – Unidentified speaker:** That's helpful. And then – and second question. In terms of the IAH 00:42:55 opportunity, you stated that you plan to launch your study the second half of this year. Can you give us more detail in terms of the potential timeline there and of that program?

00:43:09 **Answer – Unidentified speaker:** Yeah. I think it's a little bit premature to guide specifically on when we think enrollment will be completed or whatnot. We clearly will initiate in the second half of this year and have every incentive to do that as early as we possibly can. There's just a lot of work that has to go in in terms of starting up a trial, and we're well into that now, whether that's CRO selection or you know, site selection and feasibility assessments at the site level, clinical supply, placebo manufacturing, all those sorts of things.

00:43:39 So all of that is happening now. So we're well on track from that perspective. And so you will cover more. We'll provide more context as we get into it, for sure. But the team has done an excellent job to kind of ramp that up relatively quickly since the back end of last year. And we'll have more to talk about it in the near future for sure.

Unidentified speaker

00:44:03 **Question – Unidentified speaker:** Sounds good. Thanks a lot.

Operator

00:44:07 One moment for the next question. The next question comes from Oren Livnat with H.C. Wainwright. Your line is open.

Analyst:Oren Livnat

00:44:22 **Question – Oren Livnat:** Thanks. Congrats on the fast ramp here. I have a couple. Just first, I think I'm 10th in the queue here and nobody's asked about the elephant in the room, so I will. Can you talk about your statement upfront about your confidence in that – you know, whatever the jury decides, presumably any day now that your confidence in the potential of LUMRYZ? You know, why are you confident about the outcomes and what do you think the scenarios could be going forward? And also, do you have any update on timing or on the APA lawsuit that are, you know, publicly available or whatever you call you might have on that front? And then I have a follow up. Thanks.

00:45:02 **Answer – Unidentified speaker:** So the answer to your first question Oren is really easy, which is we're just not going to comment on it at this stage, that will become clear, you know, in the very near future. From that standpoint, fairly near future from that standpoint pending the jury's final decision, so I would just ask you to be patient with us on that regard. The status of the APA case I think that hearing has been moved to April 9, so that will take place on April 9 in the court in the District of Columbia, so.

Unidentified speaker

00:45:35 **Question – Unidentified speaker:** Okay. And if we try to square your commentary and near ramp with Jazz's guidance, it seems like market growth must be an important variable there. They say you're not growing the market that much yet. I think you've highlighted certainly that obviously, most of your ads are from switchers, which is, you know, as expected. But going forward through 2023 and/or 2024 and beyond, how confident are you that you can grow the market more and accelerate that growth as your products been out there longer with regards to bringing back prior discontinuers and whether those patients are identified to you or your customers and new diet patient 00:46:19?

00:46:21 **Answer – Unidentified speaker:** Yeah. Richard, you want to start on that?

00:46:23 **Answer – Unidentified speaker:** Yeah. No, sure. You know, like I said, we said before, you know what we start to see already right now to your point is the, previously discontinued segment is real and we're seeing good representation of that with in our RYZUP numbers and patients being 00:46:37 product already. We're getting new prescribers who have never written for an oxybate previous to 00:46:43 the marketplace before as well. And here's the one thing that's also a little bit challenging right now, you know, we've 00:46:49 worked hard to sort of keep our data to ourselves. So when other companies are looking at data from claims, they may not also be seeing the whole picture at this stage as well. So, you know, and what we see internally is some strong, strong early signs that people are going beyond where twice maybe oxybates were being used previously, previously 00:47:07 in the marketplace.

Unidentified speaker

00:47:11 **Question – Unidentified speaker:** That's helpful. Oh, and just one last follow-up, can you comment at all Oh, and just one last follow-up. Can you come to the -- on – I guess, net pricing or gross to net? I guess in fourth quarter or annualized in general now going forward?

00:47:33 **Answer – Unidentified speaker:** Tom. Yeah hi Oren. Yeah, we previously have got \$220,000 net revenue per patient per year. And as I've described in the past, you know, we'll get there when we reach a critical mass, which I would define as more patients continuing on therapy than the new patients coming on to therapy. With that said, I think we're rapidly approaching that point and looking forward to providing more updates on that in the future.

Unidentified speaker

00:47:59 **Question – Unidentified speaker:** All right. Thanks that's all.

00:48:01 **Answer – Unidentified speaker:** 00:47:53 that after.

Operator

- 00:48:01 I show no further questions at this time. So this will conclude our Q&A session. I would now like to turn the call back to Greg Divis for closing remarks.
- 00:48:07 Thank you and thanks, everyone for your time for joining us today on our call. And we wish you all a great day. And we certainly look forward to providing more updates here in the very near future. Thanks.

Operator

- 00:48:19 This concludes today's conference call. Thank you for your participation. You may now disconnect.

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EXHIBIT 3

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

AVDL.OQ - Q2 2024 Avadel Pharmaceuticals PLC Earnings Call

EVENT DATE/TIME: AUGUST 08, 2024 / 12:30PM GMT

AUGUST 08, 2024 / 12:30PM, AVDL.OQ - Q2 2024 Avadel Pharmaceuticals PLC Earnings Call

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PRESENTATION

Operator

Greetings, and welcome to Avadel Pharmaceuticals Second Quarter 2024 Earnings Call. (Operator Instructions) The question-and-answer session will follow the formal presentation. As a reminder, this conference is being recorded.

It is now my pleasure to introduce Austin Murtagh with Precision AQ. Thank you. You may begin.

Austin Murtagh - Stern Investor Relations - IR

Good morning, and thank you for joining us on our conference call to discuss Avadel's second quarter 2024 results. As a reminder, before we begin, the following presentation includes several matters that constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995.

Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those contemplated in such forward-looking statements.

These risks and uncertainties are described in Avadel's public filings under the Exchange Act included in the Form 10-K for the year ended December 31, 2023, which was filed on February 29, 2024, and subsequent SEC filings.

Except as required by law, Avadel undertakes no obligation to update or revise any forward-looking statements contained in this presentation to reflect new information, future events or otherwise.

AUGUST 08, 2024 / 12:30PM, AVDL.OQ - Q2 2024 Avadel Pharmaceuticals PLC Earnings Call

On the call today are Greg Divis, Chief Executive Officer; Richard Kim, Chief Commercial Officer; Dr. Jennifer Gudeman, Senior Vice President of Medical and Clinical Affairs; and Tom McHugh, Chief Financial Officer.

At this time, I'll turn the call over to Greg.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you, Austin. Good morning, everyone, and thank you for joining us for this quarterly update. Following my opening remarks, Richard will provide an update on our launch progress, Jennifer will walk through our Phase 3 idiopathic hypersomnia or IH clinical trial, Tom will then review our second quarter financial results and we will conclude with a question-and-answer session.

The second quarter marked the one-year anniversary of introducing LUMRYZ to the market, and I'm immensely proud of the work done by our team and the impact we have made within the narcolepsy community.

From the start, we recognized that oxybate-eligible patients deserve a once-at-bedtime treatment option that address their needs where first-generation oxybates fell short. Our team's relentless determination in serving people with narcolepsy has been the driving force behind our tremendous progress.

Since launch last year, we have seen our pre-approval market insights materialize in real time, which when combined with the strong foundation we have built only reinforces our confidence in the significant opportunity that LUMRYZ offers in our pursuit of its potential \$1 billion-plus opportunity.

Specifically, we point to the following. We have seen consistent strong uptake from patients switching from the twice-nightly, first-generation oxybate products, the majority coming from the mixed-salts formulation.

Demand is growing from both naive patients and patients who have previously tried and discontinued twice-nightly oxybates, a patient segment many had discounted; and the launch of LUMRYZ has resulted in the expansion of new oxybate prescribers who have previously never written an oxybate script and, additionally, physicians who are now treating more patients with oxybates, specifically with LUMRYZ, than prior to our launch, resulting in new patients coming into the oxybate market that prior to LUMRYZ were not accessible or potentially interested.

These important data points only confirm what our research informed us, that the oxybate market opportunity for LUMRYZ is both significantly larger than that of the first-generation oxybate and is unique primarily to LUMRYZ alone. With that, we are pleased to report that there were more than 1,900 patients on therapy at June 30, and we generated \$41.5 million in net revenue during the second quarter of 2024.

Additionally, as Tom will cover during his review, based upon how we exited Q2, we currently expect that we will generate operating income in Q3, an important financial milestone we will have achieved during the first full calendar year of launch.

As announced last week, we dosed our first patient in our Phase 3 REVITALYZ trial, evaluating LUMRYZ's potential benefit in the adult IH population. Based on feedback from physicians and experts in the field, we believe LUMRYZ has strong potential to improve care for those living with IH through its unique extended release formulation.

In addition, we are expecting a potential approval decision by the FDA for our supplemental New Drug Application for LUMRYZ's use in the pediatric narcolepsy population. The target action date is set for September 7.

If approved, we believe LUMRYZ has the potential to address the needs of both pediatric narcolepsy patients, who could benefit from a full therapeutic dose of an oxybate given in a once-at-bedtime formulation; and the caregivers who currently have to awaken in the middle of the night, night after night, to administer a second dose of a first-generation oxybate to their children.

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Lastly, we continue our development work on a potential no- or low-sodium, once-at-bedtime oxybate formulation with a target profile that is bioequivalent to LUMRYZ. As previously stated, we expect to have an update by the end of 2024.

In summary, after one year of launch and with an eye on the future, we believe LUMRYZ is well positioned in its pursuit to become the preferred oxybate among patients and providers as we continue to positively impact the multibillion-dollar oxybate market opportunity.

I'll now turn the call over to Richard for details on our commercial developments. Richard?

Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Thank you and good morning, everyone. As Greg mentioned, it's hard to believe that we have one year of launch behind us and what a year it's been. It has been amazing to witness LUMRYZ's transformative impact among people with narcolepsy, their families and health care providers.

Let me start with our new key piece of metric. As of the end of Q2, there were more than 1,900 patients on therapy. Additionally, for our leading indicators that we have provided quarterly since launch through June 30, approximately 3,800 patients were enrolled in our RYZUP patient support program and more than 2,400 total patients had initiated therapy.

With our second quarter numbers, you can see that we have continued the momentum with our launch and that there has been no slowdown in quarter-over-quarter patient demand for LUMRYZ.

Now, looking at our patient dynamics. We continue to have strong representation across our three patient segments including, those switching from or previously discontinued twice-nightly oxybates and those new to oxybates.

As expected at this stage, switch patients still make up a significant portion of patients on LUMRYZ. At the same time, it's been especially encouraging to see more new-to-oxybate patients being prescribed LUMRYZ.

Now, this in addition to LUMRYZ's use in previously discontinued, twice-nightly oxybate patients along with, new writers for LUMRYZ who have previously never prescribed an oxybate are important data points validating our market research that LUMRYZ can grow the oxybate market beyond its size from when it was just first-generation oxybates.

Now, our data continues to indicate, there are more than 4,500 HCPs who make up the current oxybate-prescribing universe. Importantly, from these HCPs almost 500 make up 50% of the total oxybate prescription volume. And to date, 85% of that group have written for LUMRYZ.

We are pleased with our continued capture of high-volume oxybate prescribers, as they represent a core component of our launch strategy. Transitioning to product fulfilment, our overall pull-through process continues to deliver with over 700 new patient starts in the second quarter.

These results are attributable to a number of factors including robust payer coverage, strong execution from our field reimbursement and RYZUP teams, along with HCPs continuing to gain clinical experience prescribing LUMRYZ.

Looking to the second half of the year. We have built a strong foundation; we believe will support LUMRYZ's ongoing uptake in the narcolepsy community. In particular, demand for LUMRYZ continues to be strong and our fulfilment systems are working to get patients initiated efficiently.

Paired with early signs that the oxybate market is growing, we remain highly confident in our belief that LUMRYZ is on track to become the preferred oxybate in the narcolepsy market.

And now, I will turn the call over to Jen to discuss the recent dosing of the first patient in our Phase III IH study.

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Jennifer Gudeman - Avadel Pharmaceuticals PLC - Senior Vice President, Medical & Clinical Affairs

Thank you, Richard. Since the introduction of LUMRYZ, we have heard from patients and providers repeatedly about the transformative relief LUMRYZ has brought to their lives. LUMRYZ has not only provided patients with the opportunity for an uninterrupted night sleep, but we also often hear about what they characterize as a restored ability to live their lives on their own terms.

While we have been serving the narcolepsy community for more than a year with LUMRYZ, people living with IH have been severely constrained in a lack of approved treatment. In April, an externally led patient-focused drug development meeting was held with the FDA in SLEEP consortium, to inform patient needs for IH treatment.

Among more than 800 individuals living with IH, nearly two-thirds of respondents stated that their IH symptoms were not controlled or were poorly controlled. Patient testimonials underscore the need for additional therapeutics. Physicians and patients have been vocal in their demand to see LUMRYZ evaluated for IH, due to the deep sleep inertia associated with IH and we are now answering their call.

We are excited to have recently dosed the first patient in our clinical trial evaluating LUMRYZ for IH, as it is the first step to potentially bringing this important therapy to patients. Our study known as REVITALYZ, is a double-blind placebo-controlled, randomized withdrawal, multicenter Phase III study to evaluate the efficacy and safety of LUMRYZ as a once-nightly dose in IH patients.

Enrollment of approximately 150 participants will include both those switching from first-generation immediate-release oxybates, as well as those not on oxybate therapy at baseline. Our primary efficacy endpoint is to demonstrate a change in the Epworth Sleepiness Scale score, which is administered at week 14, after a two-week double-blind randomized withdrawal period.

Our key secondary endpoints are the Patient Global Impression of Change in the idiopathic hypersomnia severity scale, which is a validated multi-domain assessment of key IH symptoms. The primary efficacy analysis will occur after the 14-week portion of REVITALYZ is completed, and the study will be followed by an open-label extension. Initiating REVITALYZ is a key milestone for Avadel and most importantly, for the IH patient and medical community.

We have seen the positive impact that LUMRYZ has had on narcolepsy and are working diligently toward expansion in IH.

I'll turn the call over to Tom for a review of our financial results.

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Thank you, Jen. Before I begin, please note that full financial results are available in the press release issued this morning and the 10-Q. I will also be reviewing non-GAAP financial results, which can be found on our Investor Relations website at investors.avadel.com.

I'll start with our top line results. In the quarter ended June 30, 2024, we reported net revenue of \$41.5 million and gross profit of \$38.7 million, both of which represent a greater than 50% increase from the quarter ended March 31, 2024.

The increase in net revenue was driven primarily by continued strong patient demand for LUMRYZ. Additionally, we estimate that there was about four weeks of inventory in the channel at the end of June versus approximately three weeks at March 31.

Turning to operating expenses. We reported \$51.5 million of GAAP operating expenses for the second quarter, which includes a nonrecurring expense of \$5 million related to the previously announced mandatory exchange of the company's American Depositary Shares and termination of the American Depositary Receipt program. As a result of the mandatory exchange, Avadel was added to the Russell 3000 Index at the beginning of July.

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The second quarter also included \$6.5 million of non-cash charges comprised of stock-based compensation of \$5.5 million and depreciation and amortization of \$1 million. After adjusting for these items, which totaled \$11.5 million, remaining cash operating expenses were approximately \$40 million.

We expect that for the remainder of 2024 recurring quarterly cash operating expenses will be in the range of \$40 million to \$45 million and non-cash operating expenses will be in the range of \$5 million to \$7 million.

With respect to the balance sheet, we had \$71.4 million of cash, cash equivalents and marketable securities as of June 30. The use of cash during the second quarter included the \$5 million of expense related to the termination of the American Depositary Receipt program.

I'll finish my remarks with a few comments regarding our expectations for the remainder of 2024. We continue to pay close attention to the sell-side estimates.

And at this time, we are comfortable with the current revenue consensus of approximately \$168 million for the full year including the possibility that it could be higher if actual results such as the rate of increase in reimbursed patients, the total number of reimbursed patients who are treated with LUMRYZ and net pricing outperform the assumptions currently used by the sell-side analysts.

Lastly with respect to our time line to reaching breakeven, we were very close to achieving this during the second quarter, when comparing \$38.7 million of gross profit to approximately \$40 million of recurring cash operating expenses, which resulted in an adjusted operating loss of approximately \$1.2 million.

Based on our current plans and assumptions, we expect that adjusted operating income will be positive, beginning in the third quarter and continue to be positive for the remainder of 2024. Our expectations regarding adjusted operating income are based on a number of factors including the number of reimbursed patients on LUMRYZ, net pricing of LUMRYZ and recurring cash operating expenses.

And with that I will turn the call back to Greg for closing remarks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you, Tom. Before we wrap up, I want to take a moment to comment on our publicly reported launch metrics and what to expect moving forward. This quarter we added a new metric. The total number of patients on therapy.

With the full year of launch now behind us going forward we intend to report only this patient metric and of course, revenue, as we believe these two metrics are the most important as our launch matures. We believe we are well positioned to execute our business priorities including our ongoing launch of LUMRYZ and our life-cycle management opportunities both of which are focused on our primary business objectives, maximizing the full value of LUMRYZ.

So in conclusion, we're very pleased with our progress and our growth thus far recognizing that we have much more to accomplish. We thank you for your support and look forward to providing future updates on our progress.

And with that, we will open the call for questions. Operator?

QUESTIONS AND ANSWERS

Operator

Thank you. At this time we will conduct the question and answer session. (Operator Instructions)

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Andrew Tsai, Jefferies.

Andrew Tsai - Jefferies Financial Group Inc. - Analyst

Hi. Good morning. Congrats on the strong launch and appreciate you sharing the metrics. Thanks for taking our question. So the first one is if we were to take another look at data cut as of July or even early August, how does the slope of uptake looks so far?

Should we be factoring in some kind of summer seasonality due to holidays occasions this quarter? Or should we expect slope of patient additions and so forth to remain unchanged or even increase this quarter? Thanks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks, Andrew. I think we would qualitatively characterize it as our trends remain consistent. As we've seen to date, this is our first summer that we've been in the marketplace. So whether there's seasonality or not, we'll have a chance to assess that for LUMRYZ specifically as we get through the period. But at this point, I think we would describe it as continuing to be consistent as to what we've seen.

Andrew Tsai - Jefferies Financial Group Inc. - Analyst

Great. And then secondly speaking of just the slope being consistent, pediatric could be approved in a month from now. So that's 5% of the current oxybate users. So is it fair to assume there could be a nice little bolus coming from that approval? Or could the uptake in the subpopulation be slower than what we're thinking? Thanks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yes. I think as we think about it, it's an important addition to our label because we hear quite a lot from parents who wake up in the middle of night, night after night. Again, it's a relatively small patient population.

So I think over time, we have an opportunity to both convert patients as well as potentially even expand the use in the pediatric market over time based upon some of our insights. I think as we think about the balance of 2024, it's modestly or marginally incremental at this point but longer term we think it's really important.

Andrew Tsai - Jefferies Financial Group Inc. - Analyst

Great. Thank you so much.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you

Operator

François Brisebois, Oppenheimer.

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François Brisebois - *Oppenheimer & Co. Inc. - Analyst*

Hi. Thanks for taking the questions. I was just wondering in terms of reimbursement where we stand now and just the impact there of if you kind of cut it as a revenue per patient and obviously, I appreciate the new metric and the look back at that new metric and what it meant ?

But if we're thinking about revenue per patient, is there any impact expected from reimbursement here in the second half?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Maybe Richard you can cover reimbursement and Tom kind of value per patient.

Richard Kim - *Avadel Pharmaceuticals PLC - Chief Commercial Officer*

Franc, thanks for the question. Yeah, we're super pleased with how our market access team has performed. Today, we have about 85% of commercially covered lives where our LUMRYZ policy exists. So it's been really strong which has really helped to drive us being able to get patients initiated.

So Tom, do you want to sort of take the revenue per patient?

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Yeah. So thanks, Frank. The revenue per patient last quarter we had talked about exiting the quarter at about \$120,000 per reimbursed patient. We've seen some improvement in that. That net pricing heading into Q2, let's say it's natural to some extent because Q1 is pretty heavily impacted by gross net adjustments. So we're -- we do see some improvement in Q2.

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

I think the only other comment I would add regarding reimbursement is that the other segment of our business which represents 15% to 20% of enrollments are really noncommercial, predominantly Medicare and Medicaid.

And as we get into 2025 where a lot of those decisions will be made for LUMRYZ which we weren't eligible in 2024 especially for Medicare, we'll get a better sense of how our coverage evolves beyond the commercial coverage as we go closer to the end of this calendar year.

François Brisebois - *Oppenheimer & Co. Inc. - Analyst*

Thank you. And then maybe just lastly in terms of new prescribers to oxybate that weren't prescribers before the 4,000 or greater than 4,500 I know it's concentrated, but did you guys approach these docs? Is it surprising that these docs who never prescribed oxybates for over 20 years have started based on the once-nightly? Is it just more awareness? Where do these docs come from?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Richard?

Richard Kim - *Avadel Pharmaceuticals PLC - Chief Commercial Officer*

Thanks, Frank. So for the vast majority of those providers, we have not called on them. So I think this really speaks to the really tremendous value proposition that LUMRYZ brings. And in our prelaunch market research when we tested our profile with high-use narcolepsy prescribers who don't

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use oxybate, half of them said with the profile of LUMRYZ they would want to prescribe LUMRYZ compared to what they haven't done with the first-generation oxybates.

So we think it's a really positive sign and something for us to build upon going forward.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yes. I'll just add to Richard's comments is that it's really interesting to us that we're getting demand without any really true effort on our part directly in terms of promotion. So it's something we're evaluating to see if it's there's some more we can do there for sure.

François Brisebois - Oppenheimer & Co. Inc. - Analyst

Great. Thank you and congrats.

Operator

Ami Fadia, Needham & Company.

Ami Fadia - Needham & Company Inc. - Analyst

Hi. Good morning. Thanks for taking my question. Can you give us a sense of what percent of patients that are currently on LUMRYZ either came from one of the other oxybates versus previously discontinued and as well as never on oxybate before? Any updates?

And then if you could give us any updates on pull-through at the payer level across the three GPOs that you have contracts with perhaps any color on Humana or some of the other Optum plans would be helpful. Thank you.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Richard?

Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Yes, thanks for the question, Ami. So as far as sort of like percentage of switch versus sort of never on an oxybate before, the biggest chunk of our patients that we have right now are still being sourced from switch patients from first-generation oxybate with the highest percentage of those being from the mixed salt overall as well.

So what we are seeing at the same time though is that the new-to-oxybate patients are starting to increase their representation as well. I mean we really see that as a very positive sign really to sort of continue to support the value proposition of LUMRYZ.

So, the biggest chunk is still SWITCH patients, but we are starting to see a bit of an increase in the representation of new patients tired of the oxybates. And as far as the GPO representation is concerned, I think traditionally what we start to see is the Zinc CVS Emisar and the -- Ascent Emisar are the biggest chunk with Optum being smaller.

And I think what we're seeing in general is the channel is being representative of the size of those GPO contracts with the Zinc being the largest Ascent being the second largest and then the Emisar-Optum business being the smallest of the three. So, pretty consistent with the sizing opportunity of those three contracts that we have.

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Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yes, I think the only other comment I would add to that is that I think it's fair to say that the significant majority of the lives underneath those GPO umbrellas have established policy coverage decisions now not all of them with regards to LUMRYZ.

So, I think getting to your question we've got policy coverage decisions in place and pulled through those through the GPO contracts.

Ami Fadia - Needham & Company Inc. - Analyst

Okay, great. If I may ask one more question can you just sort of walk us through or give us an update on the cadence of when you expect decisions from the ongoing IP cases?

And specifically on the Jazz versus FDA case can you walk us through the upside downside; and how we should think about in a downside scenario the ability to keep LUMRYZ on the market should a decision go in favor of Jazz?

Thank you.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Well, in terms of timing, I think it's our view that the next decision will likely come out of the APA case in D.C. followed by the patent case in Delaware. So, when that is? We don't know and they could come in a different order I guess but that's ultimately at the discretion of the judge from that perspective. And we -- again our position hasn't changed we're very confident in our views.

And even if the decision were unexpectedly go against us in that regard, we're prepared to take whatever steps necessary to ensure that LUMRYZ stays on the market to be able to treat patients accordingly and we believe that will be the case.

But I'll close out again on the litigation matters that we're highly confident in our position. And I'll remind all of our investors that there's other cases that are coming after this as well including our antitrust case which has been set for November of next year for which we are pursuing requisite damages for the unnecessary delay of LUMRYZ's approval due to the inappropriate listed (technical difficulty)

But in terms of timing, it's really at the discretion of the judge and we're prepared to act accordingly.

Ami Fadia - Needham & Company Inc. - Analyst

Thank you.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks Ami.

Operator

David Amsellem, Piper Sandler

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David Amsellem - Piper Sandler Companies - Analyst

Hi thanks. Just a couple for me. I know you're going to have more updates on the low-sodium product. But can you talk to generally the IP situation on that formulation and your level of confidence that you're not going to run a foul of Jazz's intellectual properties surrounding their low-sodium oxybate product? So, that's number one.

Then number two is, is it fair to say that with the bioequivalence pathway for that that there's a relatively rapid path to market for that formulation?

And then lastly on IH, are you thinking about that opportunity as something where you can expand the market? Or do you see switching away from Xywav to LUMRYZ in the IH setting? Or is it a little bit of both? Thanks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks David. I'll try to tick those off one at a time. Again, I think when it comes to our development strategy and our approach to a low- or no-sodium formulation, we have to understand what's in the past landscape for sure. And so we would be pursuing that.

Of course you should assume that we're pursuing our direction accordingly in that -- with that being considered appropriately in our development plan. If it was as simple as just formulating something similar to what's in the market today it would have already been done by now from that standpoint.

So, again, we're very conscious of what the patent landscape is out there and navigating it appropriately. Number two, on your question about the development pathway using a bioequivalence that ultimately is the decision by the FDA to agree with us on that approach.

But we do believe that there is a pathway based upon other products that have been approved that a bioequivalent-only pathway is a viable pathway assuming we can demonstrate bioequivalence and the FDA agrees with that.

And lastly, in terms of IH, I think right now you've heard Jen talk about the research and the symposium that the FDA held specifically where 800 patients talked about the need for more therapeutic options. Their symptoms are not controlled with the current available treatments.

So, from our perspective just the narcolepsy patients may choose due to the nature of this condition to want to switch to LUMRYZ to be approved.

Our view is we think it's important to add another treatment option. We think the nature of this condition is such that a once-a-bedtime option in the form of LUMRYZ is very, very compelling to patients and we hear that all the time in particular from physicians and key opinion leaders who as Jen, I think noted are very, very bullish on the prospects of what LUMRYZ could offer for their patients primarily because these patients struggle with the ability to wake up full stop, right can take their second dose.

So again, for us, it's an option for all patients whether they're on therapy today. And what we know today is that there's depending upon what data set you look at there's anywhere from 30,000 to 40,000 patients with a unique diagnosis code related to idiopathic hypersomnia and a small percentage of those are actually being treated with the only FDA-approved drug today. We think LUMRYZ offers a really great option for them as well.

So thank you.

Operator

Marc Goodman, Leerink.

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Marc Goodman - *Leerink Partners LLC - Analyst*

Tom, I know you talked (technical difficulty) about kind of the cost or anything. Can you just give us a sense of free goods? Just how much -- what percent of free goods both the second quarter maybe just the direction you're moving in there and the impact?

And just more broadly on the market, what's your sense of the total number of (technical difficulty) oxybate patients? Like how much did it grow versus before you launched?

Thanks.

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Yeah. Marc, you're a little bit breaking up. So I just want to make sure, your first question is, I believe, the patients who are on free product right?

Marc Goodman - *Leerink Partners LLC - Analyst*

Yes.

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Relative to the total. And then, the second is just how we're viewing the market trending? So

Marc Goodman - *Leerink Partners LLC - Analyst*

Yeah. How much the markets changed exactly, before you launched then now?

Richard Kim - *Avadel Pharmaceuticals PLC - Chief Commercial Officer*

Yes. I know. Thanks for the questions, Marc. For us, where we are with LUMRYZ in the launch right now we think the single-most important thing that can happen is HCPs and patients get experience with LUMRYZ. And the feedback thus far has been terrific. And we really see three products as an investment in our launch overall.

What we hear from other specialty sort of chronic product launches is sort of free products being used in about that 20% to 25% range of total patient usage. We think that's a pretty good proxy when you think about things. And for our business over 80% of our business is commercial today.

I think Greg had commented that part of our business, we would anticipate getting more of our CMS especially Medicare patients being picked up in 2025.

So we do believe that things will improve for us. But once again it really comes down to us doing free products as an investment and getting HCP and patient experience and ultimately we are also able to convert some of these patients using our programs either our bridging program or our temporary assist program our permanent affordability programs on to reimburse patients as well.

So -- and as far as the overall market size is concerned we've had -- with our claims data provider it's been a little bit messier in the second quarter for us overall. But what we see overall in the marketplace Marc is a few good leading indicators for why we believe the market is growing for oxybates.

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The first is the previously discontinued patients to twice-nightly oxybates, we believe are uniquely a LUMRYZ opportunity. And we're getting a good portion of those starting an initiating therapy with LUMRYZ.

The second is we are getting more new to naive patients initiating on LUMRYZ. That's consistent with the market research that we've heard prior to launch that LUMRYZ would open the doors for more new-to-oxybate patients considering going out on oxybate.

The third thing that we talked about earlier was that we are getting unique prescribers who had never prescribed the first-generation oxybates that are now prescribing LUMRYZ as well. So we view these as all early positive signs that the market is growing beyond where the first-generation oxybate market was.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. I just want to emphasize a couple of points, Richard made. Again, I'll just restate it. Number one is that, we don't think LUMRYZ is going to dramatically be different in terms of its percentage of free drug versus kind of other products.

But what we've seen which I think is a really positive, is we've seen patients when a coverage policy decision comes into play as Richard noted, we've been able to convert them to a in essence a paying patient. So that's something that our team is focused on. And we'll continue to do that.

And again, I think, the way I think about the notion of what's happening with the market because kind of the secondary data sources are a little choppy right now is that patients that were getting added to LUMRYZ sources of business were getting added to LUMRYZ, as new starts they're not in the denomination of kind of the legacy market, right?

Those patients weren't there before. So from our perspective that is a great sign in terms of what are the prospects one year into launch of what the potential future holds for our ability to really grow this market.

Marc Goodman - Leerink Partners LLC - Analyst

Thanks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you, Marc.

Operator

Ashwani Verma, UBS.

Fatima Amanat - UBS Equities - Analyst

Hi. Good morning. It's Fatima, on behalf of Ash Verma at UBS. Thanks for taking my question. Just like very quickly, can you talk about what you are seeing in terms of discontinuation persistence rates? Any change from what we've seen early in the launch? And just a quick second question, are you seeing any impact in the second quarter from Xyrem being removed from certain formularies? Thank you.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you very much. Richard?

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Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Yes. No. Thanks for the questions, Fatima. So as far as discontinuation, what we see holistically is LUMRYZ has lower discontinuation rates than the first-generation oxybates when we compare that at time mesh cohorts of patients through the launch.

What we do know historically is discontinuation rates for oxybate tend to be higher earlier in treatment and they tend to subside overtime. And that's also what we see with LUMRYZ once again lower than first-generation oxybates.

And the discontinuation rate is probably driven a little bit more from naive patients and previously discontinued patients that do have a higher discontinuation rate than the switch patients do over time.

But we've also learned a lot like we have in other components of our launch. We're learning a lot of -- from HCPs and patients. We're learning how to intervene differently when to intervene how to intervene how to specialize things depending on which patient type.

So we know that every product does have dropouts and that's true of any chronic medication. But we worked really hard to get these patients started and we're going to be working really hard to make sure that the right patients stay on therapy as well.

And as far as your second question about the impact from Xyrem yes I mean, clearly, there was some changes in some formularies that happened earlier this year. We did benefit from some of those patients going on to LUMRYZ.

But we also know that our value proposition is very strong against all first-generation twice-daily oxybates. So those switch patients as we mentioned before remain an important source of our business in addition to the other two segments as well as we go forward.

Fatima Amanat - UBS Equities - Analyst

Great. Thank you.

Operator

Oren Livnat, H.C. Wainwright

Oren Livnat - H.C. Wainwright. & Co. LLC - Analyst

Thanks. I appreciate it. Clearly, you have plenty of room to grow in narcolepsy but you're pretty aggressively pushing into IH. And I have just a couple of questions there. First, what's the reasoning behind trying to get in there right away now while that market is maybe not as developed?

Is there any reason to maybe let your competitor with twice-nightly continue to make the investments and do the leg work probably the tougher lifting to grow that market first and get oxybate established as a therapy versus getting in there ASAP?

And also do you believe you have IP aside a freedom to operate there given I think there's some different labeling on the Xywav side and some of the arguments your competitor is making on that front in court? And I have a follow-up there.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Oren, whatever the competitor is doing they're doing it right from that perspective. But it's clear to us and our feedback from physicians and patients that there is an unequivocal need for LUMRYZ in this category in this patient population.

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And we're not going to wait for someone else to do whatever they're going to do to serve this community and help expand and build our franchise. And regardless of what's in their label or what arguments they make or don't make, it doesn't matter to us, because we believe if we're going to introduce LUMRYZ to this patient population, it will be well received it will serve and have its rightful place and has the opportunity to make a difference. And arguably, we're the market leader in this category as well.

So, we believe, we have full rights to operate accordingly. And at the end of the day, the market has spoken to us in the form of patients and physicians, who said, get us LUMRYZ as fast as you can. That's what we're trying to do.

Oren Livnat - *H.C. Wainwright & Co. LLC - Analyst*

Okay. And it's really impressive that you guys are projecting adjusted breakeven next quarter and I think OpEx was actually lower than I had modeled excluding that item this quarter. Can you just talk about -- you're growing revenue really rapidly OpEx not so much or at all now. How does that look going forward?

Are you right-sized for continued dramatic growth from here IH aside? Or do you think you need to invest more on this product along with revenues?

And also, I'm curious about cash conversion going forward too. Obviously and it's not surprising accounts receivables are accumulating as this product grows rapidly but do you expect that to reverse in the second half?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

I'll save the second question for Tom. In terms of your comment about do we need to invest more on the launch, here's how we would describe it. Again, we're constantly evaluating our source of business and where opportunities are to try to accelerate the launch of LUMRYZ.

I would say that, we are generally well deployed and well-resourced to maximize the primary opportunity in LUMRYZ. But we are not the least bit shy of deploying more capital or investing in opportunities, if we believe it has an opportunity to really grow both the speed and the peak of what LUMRYZ can achieve from that standpoint.

So it's something, we're always looking at. I will point to the comment that we made earlier today that we're seeing patients go on LUMRYZ from physicians who we are not actively calling on. So we've been trying to understand that and what are the profile of those physicians and is there an opportunity to pursue that more aggressively and accelerate that segment?

We believe -- we've always believed longer term that was going to be something we were going to pursue overtime, but it has moved faster maybe than what we had assumed which we think is positive and it's something we're looking at.

So I think at the end of the day it doesn't change our outlook in terms of our view on profitability and generating operating income in the second half of this year and going forward. But it does -- it is something we're always looking at because at the end of the day maximizing LUMRYZ is our primary objective.

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Yes. Oren, thanks for the question. Listen, we believe we're going to hit cash flow breakeven this year. You picked up on a key point and it's not surprising that as we grow our working capital will increase primarily in the form of accounts receivable. But what you see sitting on the balance sheet at June 30, we'll convert to cash in Q3.

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Oren Livnat - *H.C. Wainwright. & Co. LLC - Analyst*

Perfect. Thanks. Appreciate it.

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Thanks, Oren.

Operator

Myriam Belghiti, LifeSci Capital

Myriam Belghiti - *LifeSci Capital LLC - Analyst*

Thank you and congrats on the quarter and launch progress. Just a quick question for me. For the Phase 3 IH study, how should we be thinking about success here? And how do you think LUMRYZ's performance will compare to data shared from the RD-approved product?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Well again I'll make some comments and Jen feel free to weigh in. I think at the end of the day we have an excellent proxy in terms of narcolepsy in terms of how LUMRYZ performed in our pivotal trial relative to the first-generation oxybates, right?

We believe that gives us high confidence that LUMRYZ will be successful in our IH trial that we've initiated. So we're highly confident that we'll demonstrate a highly statistically significant benefit to patients. And from that standpoint we remain highly confident. Anything you want to add to that?

Jennifer Gudeman - *Avadel Pharmaceuticals PLC - Senior Vice President, Medical & Clinical Affairs*

The only thing I will add is that the enthusiasm from the investigators who are participating in this trial certainly underscores everything that Greg has said. There is a long-overdue unmet need to be able to provide an extended release form of sodium oxybate for IH which only LUMRYZ will provide if it's approved.

Myriam Belghiti - *LifeSci Capital LLC - Analyst*

Got it. Thank you for taking my questions.

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Thanks, Myriam.

Operator

Matt Kaplan, Ladenburg Thalmann.

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Matt Kaplan - *Ladenburgh Thalman & Co. Inc - Analyst*

Hi. Good morning, guys. Congrats on the strong quarter results. Just to stay on the IH theme a little bit can you talk about maybe it's a little bit early since you just started the trial but the time line for the Phase 3? And then also the regulatory pathway do you think you'll need two studies?

Or will one be sufficient for an NDA filing?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

I'll take the first part of that and Jen feel free to weigh in on the second point. Matt, I think you made a good point which is that it's early in the trial. We're just getting our sites initiated -- our early sites initiated. We haven't reached our let's call it our full run rate or steady state.

We're very pleased with the fact that in a very short order from a site initiation we've seen patients move into prescreening and patients go on therapy -- go on treatment. So we're -- by the early data points we're excited about that but we haven't reached our -- if you will it's going to take a while before we're at our full capacity.

So I think it's difficult to project how long we think it's going to take. We've always said that we believe the best proxy right now is kind of how long it's taken the other products the other oxybate products to get through their Phase 3.

And that was let's just call it 15 to 18 months. We think that's the right proxy for us now. And to be clear our assessment our assumptions around that changes we'll be sure to communicate accordingly as and when we're up and running more at kind of full steam and steady state.

So in terms of regulatory pathway, Jen?

Jennifer Gudeman - *Avadel Pharmaceuticals PLC - Senior Vice President, Medical & Clinical Affairs*

Sure, happy to comment to that. We're very pleased with the engagement that we've had with the FDA. This will be a supplemental New Drug Application. And of course there's the prior precedent where there was only one pivotal trial to achieve approval in idiopathic hypersomnia.

So we very much believe that's our pathway as well.

Matt Kaplan - *Ladenburgh Thalman & Co. Inc - Analyst*

Great. Thanks.

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Thanks, Matt.

Operator

Thank you (Operator Instructions)

Brandon Folkes, Rodman & Renshaw.

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Brandon Folkes - Rodman & Renshaw - Analyst

Hi. Thanks for taking my question and congratulations on a very good quarter. Maybe just two follow-ups from earlier questions for me. Just coming back to the pediatric population how does the educational awareness compare in this population to get a patient or to get a caregiver to switch and convince them to move a pediatric patient off a therapy that may not be as good as LUMRYZ, but in their minds may be adequate perhaps compared to what they've tried in the past?

And then similarly just given the way base dosing there some sort of focus will the pediatric population be for the sales force given the runway in the added population?

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks, Brandon. Richard, do you want to comment on the pediatric opportunities?

Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Yes. As Greg said earlier the opportunity is about 5% of the overall marketplace today. For us right now when we think about sales force coverage, the vast majority of the pediatric patients are seen by physicians that we call on that treat both adults and pediatric patients today.

So incrementally we're only adding a few physicians who are specifically focused on pediatric sleep disorders. So I think our label will be very clear about the ability to switch patients as it is for adults today as well.

And we've just heard consistent feedback from providers and families about how this could really be a changer for their families because remember it's not only the patients who have to wake up but it's generally the entire family that's disrupted during the middle of the night.

So it's a modest opportunity as far as numbers or percentage is concerned, but we think it's a very important opportunity for us to execute against going forward as well. So we're super excited about the opportunity that lays ahead.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. I think the only thing I would add is that, I don't think today where we think it's going -- the market for pediatric patients is going to perform any different than how we see adults today in that physicians see patients in the ordinary course when they come in for their follow-up whether it's three times a year or twice a year or whatever it may be that the opportunity to discuss LUMRYZ will come up.

And, of course, it's imperative for us which we'll be doing is doing our related investment in marketing and awareness campaigns to the pediatric population to try to spur patient activation accordingly from a parent's perspective. But again that's no different than I think how we see the adult population today.

Brandon Folkes - Rodman & Renshaw - Analyst

Great. Thanks. And then maybe just a follow-up on the discontinuation rate. If I look at the metrics you gave and thanks for all the additional metrics, it looks like we had an additional 700 patients in the shared therapy during the quarter and an additional 500 patients on therapy at the end of the quarter.

Is that a fair way to think about obviously there's a lot of moving pieces around that but just at a higher level do you think that at this stage for every 700 patients starting therapy 500 will stay on LUMRYZ?

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Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Richard?

Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Yeah. Thanks Brandon. Right now we're still relatively early on the launch. And as we know historically more discontinuations tend to happen earlier or after a patient initiation. So we haven't really sort of got our full base of steady-state longer term usage.

So we think discontinuations are earlier in launch maybe higher represented than they are going to be later on in the launch. So I don't think we've quite got to our steady state so it's a bit dynamic right now. And it's hard to say exactly what's happened in the past will reflect the rates going forward.

We know that there will be more discontinuation rates over time, but the rates may be different going forward.

Brandon Folkes - Rodman & Renshaw - Analyst

Thanks. Very helpful. And then the last one if I may just on IH. Xywav does have the potential to dose once nightly. Do you believe LUMRYZ will take market share from both the twice-nightly patients and once-nightly IH patients? And so do you have any sense of what percentage of patients, of IH patients are currently making use of that once-nightly dosing on Xywav?

And that's it for me. Thank you.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks, Richard?

Richard Kim - Avadel Pharmaceuticals PLC - Chief Commercial Officer

Yeah. What we know right now from the Xywav label is 23% of patients were did take a single dose. Keep in mind those are patients from being in a study who are unable to take the two doses that the study started off with. And also keep in mind that the maximum dose of those patients is six grams that they can take.

We know that oxybate use for adults tends to migrate more towards 7.5 to 9 grams of total usage. So it's really one of the predominant things that we hear about our opportunity in IH is that a lot of patients are incapable of waking up to take that second dose.

And we believe that the opportunity for LUMRYZ is quite substantial from both those patients who are taking two doses and those patients who may be taking a single dose to potentially have a higher therapeutic option in LUMRYZ as well. So we really see the opportunity within the existing oxybate patients today and as Greg mentioned before to grow beyond that as well.

Brandon Folkes - Rodman & Renshaw - Analyst

Great. Thank you very much, and congratulations on the strong execution again.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thanks, Brandon.

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Operator

Thank you. I'm showing no further questions at this time. I would now like to turn it back to Greg Divis for closing comments.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you. And thank you everyone for your time in joining us today on our second quarter 2024 earnings call. We wish you all a great day and look forward to providing updates in the future.

Operator

This does conclude the program. You may now disconnect.

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EXHIBIT 4

REFINITIV STREETEVENTS

EDITED TRANSCRIPT

AVDL.OQ - Q4 2024 Avadel Pharmaceuticals PLC Earnings Call

EVENT DATE/TIME: MARCH 03, 2025 / 1:30PM GMT

MARCH 03, 2025 / 1:30PM, AVDL.OQ - Q4 2024 Avadel Pharmaceuticals PLC Earnings Call

CORPORATE PARTICIPANTS

Austin Murtagh *Precision AQ - IR*

Gregory Divis *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Thomas McHugh *Avadel Pharmaceuticals PLC - Chief Financial Officer*

CONFERENCE CALL PARTICIPANTS

Francois Brisebois *Oppenheimer & Co. Inc. - Analyst*

Oren Livnat *H.C. Wainwright & Co. LLC - Analyst*

David Amsellem *Piper Sandler & Co. - Analyst*

Myriam Belghiti *LifeSci Capital - Analyst*

David Hoang *Deutsche Bank - Analyst*

Brandon Folkes *Rodman & Renshaw - Analyst*

PRESENTATION

Operator

Greetings and welcome to Avadel Pharmaceuticals fourth quarter and business update conference call. At this time, all participants are on a listen-only mode.

Accompanying slides for this call can be found on Avadel's Investor Relations website. A question and-answer session will follow the formal presentation. As a reminder, this conference is being recorded.

It is now my pleasure to introduce Austin Murtagh with Precision AQ. Thank you. You may begin.

Austin Murtagh - Precision AQ - IR

Good morning, and thank you for joining us on our conference call to discuss Avadel's fourth quarter and full year 2024 results. As a reminder, before we begin, the following presentation includes several matters that constitute forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those contemplated in such forward-looking statements. These risks and uncertainties are described in Avadel's public filings under the Exchange Act included in the company's most recently filed Form 10-K and subsequent SEC filings.

Except as required by law, Avadel undertakes no obligation to update or revise any forward-looking statements contained in this presentation to reflect new information, future events or otherwise.

On the call today are Greg Divis, Chief Executive Officer, and Tom McHugh, Chief Financial Officer. At this time, I'll turn the call over to Greg.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Welcome, everyone, and thank you for joining us on our conference call to discuss Avadel's fourth quarter and full year 2024 earnings. Following my opening remarks, Tom will review our Q4 and full year 2024 financial results and we will conclude with a question-and-answer session.

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Many of you joined our call in January, where we provided a corporate update and preliminary unaudited financial results for Q4 and the full year of 2024. The final results released today are in line with that previous announcement, and we are reiterating our guidance for 2025.

Before Tom gets to that, I want to begin by providing some color on how LUMRYZ is doing in the marketplace and discuss our strategic and operational progress to fully capitalize on the LUMRYZ opportunity and secure our leadership in the sleep space.

We're now 18-plus months into our launch. In only a few months, we built a commercial organization, launched LUMRYZ in record time for an oxybate, approximately 4 weeks post approval. And since have added over 2,500 net patients on to LUMRYZ, which is approximately 3 times that of our nearest competitor over the same time period.

Or another way to look at LUMRYZ's uptake in the market since launch, is of the reported 3,450 total net patients added onto therapy to either LUMRYZ or the twice nightly mixed salt product since LUMRYZ's launch, nearly 75% of them are on LUMRYZ as of December 31. This reflects the strong clinical value proposition of LUMRYZ as well as the consistent demand and interest from all patient types which has been driven by nearly 2,200 unique prescribers.

Patient and physician feedback consistently highlights the value of once at bedtime dosing, a feature the FDA recognizes as clinically superior to all first-generation oxybate. Recognizing we are only 18-plus months into our launch, we still have much to achieve. However, our confidence in LUMRYZ and its \$1 billion market opportunity remains strong.

Furthermore, we are very confident that our refined commercial strategy and recent investments will accelerate our launch and advance our progress towards realizing LUMRYZ's full potential. In fact, we are seeing early signs of this shift already. Although it is still early in the year, our data and most recent trends point to promising momentum on our most important patient demand-based metrics, which are currently tracking at or above our internal expectations.

While these improvements appear to have begun taking hold during the first quarter, we expect their impact on revenues to become more apparent as we move into the second quarter and beyond as these newly added patients funnel through the system. This is encouraging both based on the underlying demand we continue to see and because it confirms that our investments and commercial focus are on point.

With that, let me recap our refined commercial strategy, including the ongoing investments to accelerate the launch, our life cycle management programs and key priorities for 2025. We continue to see broad adoption across all three patient segments, switch patients, oxybate naive and those who previously discontinued on oxybate. The growth in new to oxybate and reinitiating previously treated patients confirms that LUMRYZ is expanding the overall oxybate market, not just competing within it.

And aligning with our early launch targeting strategy, a core group of 500 early adopters have been instrumental driving nearly two-thirds of LUMRYZ patient starts to date. Yet this group represents less than 25% of the oxybate market. As such, significant growth opportunity remains across these adopters and the broader oxybate prescriber base, who are a key focus for us in 2025 and is reflected in some of our early positive trends.

Our launch strategy has built a strong foundation set up for continued growth, driven by these targeted investments to accelerate demand and optimize the LUMRYZ patient experience by achieving market leadership with the new-to-brand patients while generating growth from all patient segments and delivering sustained positive cash flow generation in 2025 and beyond.

As we enter this next phase, we're applying key learnings from the first 18 months while enhancing our commercial leadership, including the ongoing search for a new commercial leader. We have invested in the expansion of our customer-facing teams to enable greater customer specific engagement, whether it be patient, provider, caregiver or other. This includes our sales team, our field support team and our nursing support team.

These investments will expand our reach among potential LUMRYZ prescribers and enable us to deploy higher touch, more frequent and more personal support services to better help patients transition onto LUMRYZ. We've also enhanced our commercial leadership team with our two

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recently announced new hires who are both industry veterans with highly relevant experience and proven track records. They are fully focused on both driving patient demand and supporting patients through our patient services, distribution and reimbursement services, respectively.

We're pleased to see the high level of interest in Avadel for many talented and qualified commercial leaders and will provide additional organizational updates as appropriate, including the anticipated hiring of a new commercial leader.

Moving beyond LUMRYZ and narcolepsy, I'd like to provide an update on our other key initiatives we also believe will be important drivers of value creation for the company. First, enrollment is progressing and on track in our Phase 3 REVITALYZ trial evaluating LUMRYZ in idiopathic hypersomnia, or IH.

We continue to expect to complete enrollment in the second half of this year, top line data in the first part of 2026, followed by a potential NDA filing as soon as possible thereafter. IH represents a significant opportunity for Avadel as we routinely hear that LUMRYZ's value proposition can potentially have an even greater impact in the IH community.

This is primarily due to the deep sleep inertia IH patients face, which makes it challenging to wake up in the middle of the night to take a second dose and to receive the full therapeutic benefit of a twice nightly treatment.

The approximately 42,000 diagnosed IH patients under the care of physicians, less than 10% are being treated by the only FDA-approved treatment, further underscoring the need for additional treatment options. In addition to our ongoing IH trial, we are continuing our work on a once-nightly no or low sodium formulation with a target product profile bioequivalent to LUMRYZ to maximize our competitive position in the market.

Our once at bedtime no or low sodium formulation for potential appropriate oxybate eligible patients would be an additional compelling treatment option that would expand the patient population of those suffering with hypersomnia related disorders who could benefit from our proprietary technology and our patient-centric innovation.

And lastly, we remain confident in our legal strategy related to ongoing litigation. This includes the injunction case, which is pending the appellate court ruling, our antitrust case against Jazz that is currently scheduled for a jury trial in early November of this year, and our recently filed patent infringement suits reflecting our actions to protect our novel once at bedtime innovation.

To wrap up, we've made significant progress over the last 18 months and are very focused on these most important priorities that we believe will deliver on the promise of LUMRYZ. We're proud to have the opportunity to reduce the burden of narcolepsy and help avoid oxybate eligible people having to forcibly wake up in the middle of the night, night after night to treat a chronic condition using a twice-nightly dosing regimen the FDA stated is antithetical to the goal of improving sleep.

Now to translate our progress into our results and expectations, let me turn it over to Tom.

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Thanks, Greg. Before I begin, please note that full financial results are available in the press release issued this morning and the 10-K. I will also be reviewing non-GAAP financial results, which can be found on our Investor Relations website at investors.avadel.com.

Our final financial results for the fourth quarter and the full year ended in line with the preliminary results provided at the beginning of January. In the quarter ended December 31, 2024, we reported net revenue of \$50.4 million and gross profit of \$45.6 million.

Additionally, I'll note that gross profit includes an adjustment in cost of goods sold for a potential 3.5% royalty on sales of LUMRYZ related to the Delaware court memorandum and opinion issued in September of 2024.

To be clear, while this matter is pending a final resolution, it is a noncash expense. A ruling from the Delaware court is pending, and we intend to appeal the final decision, but from an accounting standpoint, we have included a noncash accrual and cost of goods sold.

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Turning to operating expenses. We reported \$48.9 million of GAAP operating expenses for the fourth quarter which includes \$5.1 million of noncash charges comprised of stock-based compensation of \$4.1 million and depreciation and amortization of \$1 million. After adjusting for these items, cash operating expenses were \$43.8 million.

With respect to cash, for the first time since LUMRYZ was launched in June 2023, the company was cash flow positive during the fourth quarter, resulting in an increase in cash of approximately \$8 million and ending 2024 with \$74 million of cash, cash equivalents and marketable securities.

And lastly, a few comments on our path to sustainable operating breakeven. During the fourth quarter, GAAP operating loss was \$3.3 million. However, after adjusting for noncash operating expenses, adjusted operating income, calculated gross profit of \$45.6 million, minus cash operating expenses of \$43.8 million was positive \$1.8 million. This marks the consecutive -- second consecutive quarter of positive adjusted operating income for the company.

I'll finish my remarks with a few comments regarding our expectations for 2025. Revenue is projected to be in the range of \$240 million to \$260 million, which at the midpoint represents a nearly 50% increase over 2024 and that patients on therapy will increase by nearly 40%.

Cash operating expenses for 2025 are expected to be in the range of \$180 million to \$200 million. And importantly, with a highly leverageable cost structure, cash flow for 2025 is projected to be in the range of \$20 million to \$40 million and that we can fund the ongoing launch and Phase 3 IH study for cash on hand and expected cash flow from operations.

Finally, just a brief comment on Q1. At this point, we are two thirds of the way through the first quarter. And based on what we are seeing, the early trends developing Q1 across key metrics are tracking in line with our internal expectations to deliver significant year-over-year revenue growth and achieve the full year guidance. We are encouraged by these developing trends. And as Greg noted, we expect to see this translate into improvements in revenue in the second quarter.

With that, I will turn the call back to Greg for closing remarks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you, Tom. Before we open the floor for Q&A, I'll summarize where Avadel stands today. LUMRYZ has started 2025 with positive momentum as we continue to make progress during Q1 across our key patient metrics. We're investing strategically to accelerate launch execution throughout all of 2025 and beyond which positions us for a cash flow positive 2025, while making important progress in maximizing the full potential of LUMRYZ.

Our life cycle management programs are advancing with the goal of expanding the oxybate market opportunity significantly. And all of this is supported by a robust and growing intellectual property portfolio that protects LUMRYZ into early 2042, and we will continue to vigorously protect and to defend.

LUMRYZ continues to offer a high-growth and high-value opportunity built on a highly leverageable cost structure, which we believe will deliver significant cash flow and EPS growth over time.

We remain both confident and optimistic about LUMRYZ's prospects in 2025 and beyond. We look forward to sharing commercial and key company progress updates throughout the year. We thank you for joining us in your time today and as always for your support.

We will now open the line for Q&A.

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QUESTIONS AND ANSWERS

Operator

(Operator Instructions) François Brisebois, Oppenheimer.

François Brisebois - Oppenheimer & Co. Inc. - Analyst

In terms of the sales reps, can you just remind us maybe the evolution of numbers of sales reps and where you're at now? And then any thoughts about DTC? Or is this just a little different given it's more of a rare disease? And then I have a follow-up.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. Thanks, Frank. In terms of our customer-facing roles, including our sales reps, we had about a 15% increase in our sales team that was fully effective as of 1/1/25. That number is now at 53%. And we've basically doubled the size of our field support team that is also effective as of 1/1/25 and that is now up to 28%. And then we've doubled the size of our nurse support team that's fully operational as of 1/1 as well, which also takes it to right at 28%.

In terms of your comments about DTC and what I'll just characterize as patient education through media, we've made a fairly significant increase in both our channels and our investments beginning here in Q1.

And it's important in terms of educating and reaching out and connecting and activating patients where they are and where they seek their information. So we spent a lot of time to understand that over the course of the last 18 months, and we've increased our investment in that area as well.

François Brisebois - Oppenheimer & Co. Inc. - Analyst

Okay. Great. And then on the field support and then the nurses, you just -- what is -- how different are these two? You doubled up on field support. Can you just help us understand what exactly field supports responsibility is?

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah, it's really twofold, and they're really customer-facing roles in terms of the physician audience and their offices and their practices. They work on patient pull-through from the point of prescription becoming active through the point in time when they're on therapy and are following up with the offices, in particular in and around refill times for patients.

So think of them as post prescription is written to help process the patient through the reimbursement process. And then once the patient is on therapy, they have the opportunity to communicate and engage with their office staff around where the patient is on their treatment and in particular in and around the refill of their upcoming refills or subsequent dose titration.

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Yeah. Maybe, Frank, I'll add to that. These are the targeted investments we described last year, fully operational, as Greg noted, 1/1/25, but these are the types of investments that we see as contributing to the early trends we're seeing now in 2025 and as they continue to take hold, become more effective, it should naturally lead to more patients on therapy and higher revenue.

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Francois Brisebois - *Oppenheimer & Co. Inc. - Analyst*

Is there a part -- like you talked about a couple of different forces here between the field force, with nurse support, the DTC effort, the reps, is there one of these -- like which one is most important to get to the switch patients and increase the number of switch patients? Or is it just an effort of all them together?

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Yeah. We think it's a cumulative effect of the full approach with all resources, given our sales force really started at the very top of the funnel and then our reimbursement team really pulls them through and then our media strategy meant to educate and activate patients to go in and to talk to their patients or their physicians about it.

So I think they're all important in that regard to not only make sure we're driving the right sort of patients into the top of the funnel. But as they go through the funnel, we're working and doing the things necessary to keep them on therapy.

And as Tom noted and we've noted in our commentary, the early trends in terms of the byproduct of these investments are favorable relative to where we thought we'd be at this stage. And that is a very confirming sign that the investments are the right approach. And then as these trends become more durable and sustainable, but certainly lead to an uplift in net -- the most important metric, which is net patients on therapy and revenue potentially.

Operator

Andrew Tsai, Jefferies.

Unidentified Participant

This is John on for Andrew. Any additional color on the Q1 patient trends that you can share? And then how should we think about gross to net inventory for Q1 as it relates to your Q1 sales? You saw a sizable draw -- I'm sorry. No, go ahead.

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

No, I understand the question. John, I'll take the first part and then let Tom answer the second. Again, I think what we've seen coming off of the trends in Q4 and in the second half of last year has been -- regardless of the metric you're looking at, whether it's the top of the funnel metrics in the form of enrollments or patient starts or even as we think about as patients go into therapy, all of those trends are favorable for us relative to how we've seen the year start versus internal expectations and the trends we saw through the back half of last year.

So all of that, we think, is both favorable from an underlying demand and growth potential perspective. And as those things progress through -- patients progress through the funnel, so to speak, we would expect to see some of that impact begin to take effect in Q2.

But it's also confirming from our perspective in terms of the strategy and where we're deploying our resources and the focus of the organization, including our breadth of -- our targeting more prescribers to expand our prescriber base while we continue to work on those who have been the fastest adopters of LUMRYZ as well. So I'll turn it to Tom on inventory.

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Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Yeah, certainly. So thanks for the question. Listen, I think in terms of gross to net, it's always highest in the first quarter. That's not unique to Avadel, it's true for any company operating in our space. It's primarily impacted by patient dynamics, if you will, primarily in the form of insurance deductibles resetting and we provide financial systems to the patients to make sure they continue the therapy on LUMRYZ.

With your question on inventory, what we have seen so far in the quarter, and keep in mind, we're two thirds of the way through the quarter. But the quantity of inventory in the channel has remained consistent from where it was at the -- as we exited 2024.

Operator

Ami Fadia, Needham.

Unidentified Participant

This is [Buena] on for Ami. Can you remind us of the pushes and pulls in your guidance range? What have you assumed for the low end of the guidance? And what do you believe needs to happen for you to get to the high end of the guidance range? And could that be upside to the upper end of that range?

And so how do you see first quarter sales related to fourth quarter? Will it be flat or slightly down given the first quarter resets? And the last one, after an additional two months since the January update, what are you seeing in terms of patient mix between switches and new to oxybate?

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. Thanks, Buena. On the first question, and I would just describe in terms of key drivers of the forecast and mix of patients, they're really interchangeable because the two most important metrics -- the most important underlying metric is net patients on therapy and that is a byproduct of more patients at the top of the funnel and keeping patients on therapy.

So if we have more demand overall and if that demand -- the mix of that demand skews towards switch patients, as an example, from where it was trending at the end of Q4, then all of that will likely -- and our persistency efforts continue to show promise like they have early in this year, all of that will lead to upper ends of -- upper ends of the guidance range or beyond the upper end of the guidance range. So ultimately, those are the most important metrics in terms of patient starts, net patients on therapy and then -- and the ability to keep them on therapy.

In terms of your commentary, and then I'll let Tom maybe comment on the second question, but your question on what we've seen in terms of mix of patients early on in the course of this quarter, in particular, around switch patients. Our commentary around all patient metrics, including switch patients, really holds true for all of them, right?

And the favorability we've seen across these trends early in the quarter includes the signs of both stabilizing and beginning to reverse what I would just describe as the declining switch patient trend at the end of last year.

So again, I think we feel really good about the early signals and the progress we're making. We expect that to translate into -- its impact beginning to be felt from a revenue standpoint in Q2, but it's confirmatory of where we're focused and what we're doing.

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Yeah. Certainly, listen, maybe just a follow on to the guidance, then I'll get to your question around Q1. With what we're seeing so far, and again, these are early trends, but all positive in line with our expectations. We have a clear line of sight to achieving the guidance that we had articulated

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at the beginning of January. Specifically with respect to Q1, maybe just a follow-on to my previous comment to Frank, is that what we're seeing so far in Q1, we're pleased with the early developing trends.

The -- you have to remember that Q1 is very dynamic in terms of gross to net. It's going to be higher in Q1 than it is in subsequent quarters. So we're certainly keeping a close eye on that as we progress through the quarter.

Operator

Oren Livnat, H.C. Wainwright.

Oren Livnat - H.C. Wainwright & Co. LLC - Analyst

All right. Jazz has obviously switched a lot of their XYREM franchise over to XYWAV. Some more recently, many of those patients switched a long time ago. Can you just talk about, I guess, your messaging and the feedback you get from physicians with regards to switching patients, whether they have been on low sodiums that way for a long time versus more recent switchers? Is it appreciably easier to switch somebody who wasn't switched more recently, I guess, for obvious reasons?

And then when we just talk about hurdles to switching, how is your insurance coverage relative to the competitor? Has that changed appreciably in the new year? And maybe can you talk about whether there is a difference between your actual coverage and perceived coverage out there. Is there any fear real or imagine that switching patients would result in them not being able to smoothly get on to XYWAV such that they're afraid to switch and risk disruption in their therapy?

And I have one follow-up there.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. Kind of working in reverse order. From a coverage standpoint, our commercial coverage is greater than 90% now. We have no coverage status and reimbursement access and greater than 90% of all commercial lives. We've seen -- and that's fairly comparable to our competitors.

We've seen improvements in our Medicare coverage this year. And I would view that as fairly comparable to our competitors as well. We have very little to no coverage in Medicaid, primarily because of the penny pricing that exists in the marketplace today. But over 80% of this market, 82% to 85% of this market is commercial. So we believe we're well positioned from a competitive standpoint.

Like many products early in their launch, it is a fairly standard objection you receive around the perception that access may be difficult, or you don't have the same coverage as an established product. That's something we continue to sell through and communicate and engage with to change if those perceptions exist at any individual physician level.

By and large, when we've seen switch patients get prosecuted, we haven't seen a significant hurdle or challenge for the most part in terms of being able to effectively drive to switch and deliver switch through the payer or the reimbursement process. There will be steps they have to go through to get coverage, but those are pretty well laid out. And for the most part, those patients will have met all of the static criteria that would exist before being able to go on to an oxybate given the parity coverage we have today from that standpoint.

In terms of the demographic or the type of patient who has switched or is switching and where they are in their kind of treatment journey of being on an oxybate, it really -- I wouldn't say there isn't really one core demographic, whether they've been on oxybate for a long time or a shorter period of time. We certainly, early in the launch, saw patients switching who we would describe as much more dynamic patients who are looking -- I would say, early adopting patients who are looking for the next therapy, so to speak.

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Today, as we see switches come in, they come in all different forms, different demographics, different lengths of therapy and different reasons for why they want to consider the switch. So for us, the key to that is to stay vigilant in our commercial efforts and our promotional efforts around the reasons to switch and the opportunities to switch from that standpoint.

So that's an important thing that we're focused on this year and how we built the management programs around that and the commercial programs around that to ensure that switch is an important messaging for us in particular, not only where we have strong adoption, but in the larger part of the market where we're really focused in expanding our reach and our impact. So I appreciate the question.

Oren Livnat - *H.C. Wainwright & Co. LLC - Analyst*

Okay. And just quickly, you did mention litigation. I don't know if Jared or anyone wants to comment more on any of these even on the call. But with regards to your expectations on timing and next steps, how long do you expect to hear anything back from the appellate court post oral arguments at the beginning of the month?

And do you also have any expectations around the royalty determination and the timing of next steps as we can think about sort of how long that process will take to work itself out one way or another?

Thomas McHugh - *Avadel Pharmaceuticals PLC - Chief Financial Officer*

Hey, Oren, it's Tom. So I'll take the last part of your question there. The hearing was on February 7 with respect to the [IV] conjunction, we expect to -- we don't have exact time frame, of course, it's up to them to decide when to issue ruling, but we have an expectation within two or three months following that hearing. On the royalty decision, it's -- I would just simply describe as pending at this point. All parties have submitted the judge what he had asked and he -- we are just awaiting a ruling at this point.

Operator

David Amsellem, Piper Sandler.

David Amsellem - *Piper Sandler & Co. - Analyst*

Just got a couple. Maybe this is sort of a backward-looking question. But do you feel like with the sales organization initially after the launch there was just a lot of low-hanging fruit in terms of pent-up demand and maybe a more robust switch market, and you found that the sales organization is just going to have to work harder to get that incremental patient or at least get more switch patients? So that's number one. And then maybe with that in mind, can you just talk about how you feel about the performance of the sales organization, particularly these past couple of months since the guide.

And then secondly, I wanted to get your thoughts on just the long-term implications of the orexin, which is sort of an elephant in the room here, at least long term? And how are you thinking about the oxybate market or the direction of the oxybate market in narcolepsy specifically? Do you feel like you'll be in a position to hold on to patients? Do you expect pressure where you're going to need to make up for that from IH adoption? Just help us better understand how you're thinking about the business over the long term in an orexin agonist world.

Gregory Divis - *Avadel Pharmaceuticals PLC - Chief Executive Officer, Director*

Yeah. Thanks, David. To your first round of questions around the sales force, I'm really proud of the way they've embraced the expansion of our commercial strategy and the focus of our commercial strategy over the last couple of months. The trends have demonstrated that in terms of what we see happening across our primary field-based, demand-based metrics. Really around what happens at the top of the funnel and at the bottom of the funnel.

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Inevitably, we've over-indexed early in the launch in what we characterize as adopters. And we probably had some low-hanging fruit, but we've also been quite successful in that audience. And now we're expanding our efforts into the broader oxybate prescriber base, and we're seeing early signs of expanding our reach and impact there as well. So I'm proud of our sales force and the efforts that they're delivering right now and feel really good about the momentum that they are creating specifically.

In terms of your question on orexin, there's clearly a lot of investor excitement about the prospects of orexin. What we are most interested in is the clinician and prescriber perspective. So it's certainly an exciting new mechanism of action that -- for these serious sleep conditions with clear benefit on the daytime. It's a little less clear what their benefits at night are and whether those are positive or whether in fact they may lead to some potential concerns.

But we certainly believe that there's going to be role of use of oxybate as a night time agent that also helps consolidate sleep and produces additional daytime benefits as our data says. Our goal is to make sure LUMRYZ is that oxybate of choice.

So we've been investing a lot of time in this and really talking and researching with hundreds of physicians in this regard. And our expectation is that there will continue to be listening to physicians. There will continue to be a role of oxybate and our goal is to make LUMRYZ that oxybate of choice.

Operator

Marc Goodman, Leerink Partners.

Unidentified Participant

This is [Madhu] on the line for Marc. Just a couple from us as well. Just curious, are there specific geographic regions where there are lower rates of cardiovascular comorbidities in the narcolepsy population, where your once-nightly could be more attractive than the low sodium option and where you could expect to capture greater market share in? And then also just curious if you can share any specific initiatives that you are planning to implement to increase persistency in the new to oxybate patients?

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. Thanks. Maybe I'll take the questions in reverse. From a persistency standpoint, we have obviously spent a lot of time identifying where these discontinuation risks are, and we've introduced very targeted programs to try to intervene and engage specifically with patients, prescribers through data and with the goal of really meeting the patient with the right message at the right time. And again, early in the quarter, but we've seen positive signs so far of those initiatives across our different investments.

In terms of your question about CV risk geographically or whatnot. What we can say on that topic is we've now conducted a number of research projects with closed integrated healthcare systems and CV risk in terms of patients with narcolepsy, people with narcolepsy, doesn't show up in the top 20 comorbidities and relative to the controlled cohort of the standard patient population. We know there is a percentage of patients overall that we -- that physicians talk about to us in the 10% to 15% range. You may have some sodium sensitivity or other matters.

But I can't tell you that there's a geographic area around that. We haven't seen a geographic disposition one way or the other from that perspective. What we know is that once nightly dosing is viewed as a highly important attribute for people who suffer from a chronic sleep disorder. And over the last 18 months, we have outpaced the patient starts 3 to 1 to the next nearest competitor. So we're pleased with the early trends we've seen in 2025 and continue to build -- and we plan to continue to build on that momentum.

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Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Yeah, maybe I'll just add. Persistency, listen, it's important across all patient segments. And as we continue our initiatives, we believe we're working on the right things, doing the right things. And as we continue to drive those improved persistency, it just again, it's one of those metrics and naturally leads to an improvement in revenue throughout the year.

Operator

Myriam Belghiti, LifeSci Capital.

Myriam Belghiti - LifeSci Capital - Analyst

As you're targeting the broader prescriber base, many are writing for oxybate for the first time, how are you thinking about converting these physicians to regulate this [fabric of LUMRYZ]? Do you have any specific feedback in that group, in particular, the one-off prescribers?

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. From a market expansion perspective, Myriam, it's another really great example of what LUMRYZ is bringing to the oxybate category in totality. We've seen well over 200 physicians who have never written an oxybate before now prescribe LUMRYZ and many of them have written for more than one, some have written quite a few.

So from that perspective, it really is. It's organic in terms of what's happening because these physicians are kind of signing up by enrolling in our REMS program, which gives us a trigger that they want to use LUMRYZ. What we've done in terms of our sales force expansion is to try to identify physicians who look a lot like those physicians and expand our reach into a new audience to try to, if you will, generate even more new oxybate prescribers. But we're pleased with what we've seen so far, and it's a great signal in terms of the ability to grow the market.

Myriam Belghiti - LifeSci Capital - Analyst

Okay. Makes sense. And one last question. In terms of goal for patient mix for 2025, do you have an ideal ratio in mind for which new to oxybate population mix? Is there a good goal in terms of population mix for 2025?

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

Myriam, it's Tom. So listen, we have certainly set our internal goals, how we're tracking so far is clearly inclined with our internal expectations, two months into the year. Our goal is not just to improve patient mix. It's also to drive overall demand as we referred to the top of the funnel. All these initiatives, whether it be top of the funnel, patient mix, persistency, all are designed to continue to improve revenue throughout the year.

Operator

David Hoang, Deutsche Bank.

David Hoang - Deutsche Bank - Analyst

So I just wanted to ask a little bit about your efforts to improve persistency in the naive or new-to-brand patients. So what specifically can you do there? And what would you expect the long-term persistency and discontinuation rates to look like for those patients? Do you think it would be in line or better than the twice nightly oxybate?

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Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah, David, we covered that on a number of questions, but let me just give you a little bit more perspective. In terms of our efforts from a persistency standpoint, we're really focused in 3 different areas. One is our direct engagement with patients through our nurses. Two, our direct engagement with office staff around patients on therapy. And three, supporting persistency with our pharmacy partners.

So whether you're new to oxybate, a switch patient or another one, we're trying to -- we're intervening with all those patients. And again, even through this part of the launch, we -- our persistency rates certainly look better than the legacy twice-nightly first-generation products but from our viewpoint, that's not good enough, and we're continuing to make strides to improve it.

And early -- so far this year, we're seeing some positive signs of those interventions. And if those -- and as those trends continue on and became sustainable and durable, we would expect to see that result in more net patients on therapy, which will result in an uplift in revenue.

Operator

Brandon Folkes, Rodman & Renshaw.

Brandon Folkes - Rodman & Renshaw - Analyst

I do want to follow up on a question that's been asked, I think, twice already. But you mentioned you're seeing very good trends in 1Q, and you expect this to translate into revenue growth in the second quarter. I appreciate the industry headwinds that we all see in 1Q.

But I just want to be clear here, I'm wondering, are you implying that we should consider the potential of a sequentially down quarter-on-quarter revenue quarter and 1Q over 4Q? Or can you rule this out at this stage given sort of the early indicators that you're seeing from what you've put in?

Thomas McHugh - Avadel Pharmaceuticals PLC - Chief Financial Officer

So Brandon, it's Tom. Let me start on that. So for the first time since LUMRYZ launched, we provided revenue guidance. And granted it was for the full year in the range of \$240 million to \$260 million. We're -- we haven't provided quarterly guidance.

I don't intend to at this point. Stay tuned for future quarters as we evaluate the ongoing market dynamics. Appreciate you recognizing the Q1 dynamics occur for any company in our space, particularly around gross to net. It's a very high quarter in terms of gross to net. And obviously, we're monitoring it and keeping a close eye on it but that's where we stand at the moment.

But again, I think what's important for us is the initiatives we laid out, what we're working on, which should lead to continued improvement throughout the year. And for us, at this point, a high level of confidence and a clear line of sight to achieving the guidance we provided.

Brandon Folkes - Rodman & Renshaw - Analyst

And I do appreciate all the color. Maybe just one follow-up. Any color on the pediatric indication, just sort of how that launch is going to date and how you're thinking about its contribution in '25? And then that's it for me.

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Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Yeah. It's clearly a focus. We've added some more physicians who are exclusively pediatric prescribers or pre-pediatric treaters, and we've got really great stories of parents and families benefiting from the introduction of LUMRYZ with a formal approval and being able to get clear coverage from that standpoint. It's a relatively small percentage of patients overall. And in terms of the total market, given just how the diagnosis of patients occur, it can take up towards of 8 to 15 years from onset of symptoms to a formal diagnosis which most patients are in their 20s or 30s when that occur.

So -- but we are focused on it. We've got very specific segmentation within each of our respective geographies. And pursuing it accordingly, and we're proud to be able to offer to this patient population as well.

Operator

That concludes today's question-and-answer session. I'd like to turn the call back to Greg Divis for closing remarks.

Gregory Divis - Avadel Pharmaceuticals PLC - Chief Executive Officer, Director

Thank you, and thank you, everyone, for joining us and really appreciate your time this morning. Look forward to our follow-ups through the course of today and this week and have a great day. Thank you.

Operator

This concludes today's conference call. Thank you for participating. You may now disconnect.

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EXHIBIT 5



Avadel Pharmaceuticals Announces Favorable Ruling in Appeal of Delaware Court Injunction

May 6, 2025 at 12:30 PM EDT

- With this ruling, Avadel can seek and be granted FDA approval for LUMRYZ in Idiopathic Hypersomnia -

- Federal Circuit decision permits new clinical trials and further development of LUMRYZ™ for the treatment of indications beyond narcolepsy -

DUBLIN, Ireland, May 06, 2025 (GLOBE NEWSWIRE) -- **Avadel Pharmaceuticals plc (Nasdaq: AVDL)**, a biopharmaceutical company focused on transforming medicines to transform lives, today announced that the United States Court of Appeals for the Federal Circuit (the "Federal Circuit") has ruled in favor of Avadel, overturning important parts of the injunction imposed by the U.S. District Court for the District of Delaware (the "Delaware Court") regarding LUMRYZ™ as a potential treatment of indications beyond narcolepsy.

The Federal Circuit vacated the portion of the injunction that prohibited Avadel from applying for FDA approval of LUMRYZ for any indication beyond narcolepsy, calling the district court's analysis "simply too speculative and tenuous." Additionally, the Federal Circuit lifted the portions of the Delaware Court's injunction that prohibited Avadel from offering open-label extensions to trial participants using LUMRYZ and from initiating new clinical trials or studies with LUMRYZ for potential indications beyond narcolepsy.

"We are pleased with the Federal Circuit's decision, which paves the way for Avadel to initiate new clinical trials, offer open-label extensions in clinical trials, and ultimately seek FDA approval of LUMRYZ in IH as well as other indications," stated Greg Divis, Chief Executive Officer of Avadel. "We remain relentlessly committed to demonstrating the clinical value of our differentiated, extended-release, once-at-bedtime medication."

Patient enrollment in Avadel's REVITALYZ™ trial remains on track to be completed by the end of 2025. REVITALYZ is a double-blind, placebo-controlled, randomized withdrawal, multicenter Phase 3 study designed to evaluate the efficacy and safety of LUMRYZ given as a once-at-bedtime dose, in IH. The study will enroll approximately 150 adults who are diagnosed with IH and is open for participants switching from immediate-release oxybates and to those not currently taking oxybates.

About LUMRYZ™ (sodium oxybate) for extended-release oral suspension

LUMRYZ is an extended-release sodium oxybate medication approved by the FDA on May 1, 2023, as the first and only once-at-bedtime treatment for cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. On October 16, 2024, LUMRYZ was additionally approved as a once-at-bedtime treatment for cataplexy or EDS in pediatric patients 7 years of age and older with narcolepsy.

The FDA approval of LUMRYZ was supported by results from REST-ON™, a randomized, double-blind, placebo-controlled, pivotal Phase 3 trial in adults with narcolepsy. LUMRYZ demonstrated statistically significant and clinically meaningful improvements in the three co-primary endpoints: EDS (MWT), clinicians' overall assessment of patients' functioning (CGI-I), and cataplexy attacks, for all three evaluated doses when compared to placebo.

With its approvals in May 2023 and October 2024, the FDA also granted 7 years of Orphan Drug Exclusivity to LUMRYZ for the treatment of cataplexy or EDS in adults with narcolepsy and in pediatric patients 7 years of age and older with narcolepsy (respectively) due to a finding of clinical superiority of LUMRYZ relative to currently available oxybate treatments. In particular, the FDA found that LUMRYZ makes a major contribution to patient care over currently available, twice-nightly oxybate products by providing a once-nightly dosing regimen that avoids nocturnal arousal to take a second dose.

About Avadel Pharmaceuticals plc

Avadel Pharmaceuticals plc (Nasdaq: AVDL) is a biopharmaceutical company focused on transforming medicines to transform lives. Our approach includes applying innovative solutions to the development of medications that address the challenges patients face with current treatment options. Avadel's commercial product, LUMRYZ, was approved by the U.S. Food & Drug Administration (FDA) as the first and only once-at-bedtime oxybate for the treatment of cataplexy or EDS in patients 7 years of age and older with narcolepsy. For more information, please visit www.avadel.com.

Avadel intends to use its Investor Relations website as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company's Investor Relations website, in addition to following the Company's press releases, SEC filings, public conference calls, presentations, and webcast.

IMPORTANT SAFETY INFORMATION

WARNING: Taking LUMRYZ™ (sodium oxybate) with other central nervous system (CNS) depressants, such as medicines used to make you fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope) and death.

The active ingredient of LUMRYZ (sodium oxybate) is a form of gamma hydroxybutyrate (GHB), a controlled substance. Abuse or misuse of illegal GHB alone or with other CNS depressants (drugs that cause changes in alertness or consciousness) have caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma and death.

Call your doctor right away if you have any of these serious side effects.

Because of these risks, LUMRYZ is available only by prescription and filled through certified pharmacies in the LUMRYZ REMS. You must

be enrolled in the LUMRYZ REMS to receive LUMRYZ. Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

INDICATIONS

LUMRYZ (sodium oxybate) for extended-release oral suspension is a prescription medicine used to treat the following symptoms in patients seven years and older with narcolepsy:

- sudden onset of weak or paralyzed muscles (cataplexy)
- excessive daytime sleepiness (EDS)

Do not take LUMRYZ if you take or your child takes other sleep medicines or sedatives (medicines that cause sleepiness), drink alcohol or have a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep LUMRYZ in a safe place to prevent abuse and misuse. Selling or giving away LUMRYZ may harm others and is against the law. Tell your doctor if you or your child have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Anyone who takes LUMRYZ should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery or flying an airplane, for at least six (6) hours after taking LUMRYZ. Those activities should not be done until you know how LUMRYZ affects you.

Falling asleep quickly, including while standing or while getting up from the bed, has led to falls with injuries that have required some people to be hospitalized.

LUMRYZ can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing and/or short periods of not breathing while sleeping (e.g., sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they take LUMRYZ.
- **Mental health problems**, including confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness and difficulty concentrating. Tell your doctor if you or your child have or had depression or have tried to harm yourself. **Call your doctor right away if you or your child have symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you or your child start sleepwalking.

Tell your doctor if you or your child are on a salt-restricted diet or have high blood pressure, heart failure or kidney problems. LUMRYZ contains a lot of sodium (salt) and may not be right for you. The most common side effects of LUMRYZ in adults include nausea, dizziness, bedwetting, headache and vomiting. Your side effects may increase when you take higher doses of LUMRYZ. The most common side effects in children include nausea, bedwetting, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking. LUMRYZ can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of LUMRYZ.

For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit <http://www.fda.gov/medwatch>, or call 1-800-FDA-1088.

Please see full Prescribing Information, including BOXED Warning.

Cautionary Disclosure Regarding Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects or other events. Such forward-looking statements include, but are not limited to, expectations regarding the litigation involving Jazz Pharmaceuticals Inc., including the potential benefits of the Federal Circuit's ruling; the Company's IH clinical study for LUMRYZ, including enrollment and timing related thereto; the Company's ability to offer open-label extensions and initiate new clinical trials for LUMRYZ in indications beyond narcolepsy; and the Company's ability to seek and obtain FDA approval for, as well as, commercially launch LUMRYZ for indications beyond narcolepsy. In some cases, forward-looking statements can be identified by use of words such as "will," "may," "could," "believe," "expect," "look forward," "on track," "guidance," "anticipate," "estimate," "project," "next steps" and similar expressions and the negatives thereof (if applicable).

The Company's forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company's business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company's business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company's forward-looking statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of the Company's most recent Annual Report on Form 10-K and subsequent filings with the Securities and Exchange Commission.

Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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Page 1 IN THE MATTER OF ----- ADAVDEL PHARMACEUTICALS ----- TRANSCRIPTION OF Q1 2025 Earnings Call May 7, 2025 JANE ROSE REPORTING 74 Fifth Avenue New York, New York 10011 1-800-825-3341 Wendy Sawyer, Transcriptionist FINAL COPY JANE ROSE REPORTING 1-800-825-3341	Page 3 1 March 3rd, 2025, and subsequent SEC filings. 2 Except as required by law, Avadel undertakes 3 no obligation to update or revise any forward looking 4 statements contained in this presentation to reflect 5 new information, future events, or otherwise. 6 On the call today are Greg Divis, Chief 7 Executive Officer, and Tom McHugh, Chief Financial 8 Officer. I'll now turn the call over to Greg. 9 MR. DIVIS: Welcome, everyone, and thank you 10 for joining us to discuss Avadel's First Quarter 2025 11 results. On today's call, I will provide insights and 12 commentary on the drivers of our performance during Q1 13 and the outlook for the remainder of this year. I'll 14 conclude my opening remarks with additional company 15 updates that we believe will further strengthen and 16 accelerate our business in the future. Tom will then 17 provide an overview of our financial performance and 18 guidance, and we'll wrap up with a Q&A session. 19 To start, let me underscore our continued 20 confidence in LUMRYZ, which saw accelerated patient 21 adoption and expanded physician prescribing throughout 22 the First Quarter of 2025, further, building on our 23 early launch momentum. We are pleased with the strong 24 progress we made during the first quarter of the year 25 and remain confident in our ability to continue to
Page 2 1 (Beginning of Audio Recording.) 2 OPERATOR: Greetings and welcome to Avadel 3 Pharmaceuticals, First Quarter 2025 Earnings Call. At 4 this time, all participants are in a listen-only mode. 5 Accompanying slides for this call can be found on 6 Avadel's Investor Relations website. A question-and- 7 answer session will follow the formal presentation. 8 As a reminder, this conference is being 9 recorded. 10 It is now my pleasure to introduce Austin 11 Murtagh with Precision AQ. Thank you. You may begin. 12 MR. MURTAGH: Good morning, and thank you 13 for joining us on our conference call to discuss 14 Avadel's First Quarter 2025 earnings. As a reminder, 15 the following presentation includes several matters 16 that constitute forward looking statements within the 17 meaning of the Private Securities Litigation Reform 18 Act of 1995. 19 Forward looking statements are subject to 20 risk and uncertainties that could cause actual results 21 to differ materially from those contemplated in such 22 forward looking statements. These risks and 23 uncertainties are described in Avadel's public filings 24 under the Exchange Act, included in the form 10K for 25 the year ended December 31st, 2024, which was filed	Page 4 1 deliver on our growth plan. Accordingly, as noted in 2 our press release, we raised our full year guidance. 3 We are equally pleased with yesterday's 4 favorable decision from the Federal Circuit Court of 5 Appeals regarding our ability to pursue indications 6 for LUMRYZ beyond narcolepsy. The Court of Appeals 7 rejected key elements of the Delaware trial court's 8 injunction that had prohibit us from applying for FDA 9 approval for LUMRYZ for any indication beyond 10 narcolepsy, from offering open label extensions to 11 trial participants using LUMRYZ, and from initiating new 12 clinical trials or studies with LUMRYZ. 13 This is a clear win for Avadel and for 14 patients, as we are now able to proceed with the 15 development of LUMRYZ for additional indications, 16 conducting clinical studies, and seeking FDA approval 17 for those indications, including IH. 18 Since the beginning of 2025, we have seen 19 improvements across our key launch metrics for LUMRYZ, 20 including patient enrollments, new patient starts, 21 persistency rates, and most importantly, the 22 accelerated growth of net new patients on therapy. 23 This progress reflects the investments we 24 have made in strengthening our leadership team, 25 refining our commercial strategy, providing additional

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1 patient support, expanding our customer facing roles, 2 and as such, expanding our provider and patient 3 engagement. 4 While we are pleased with these promising 5 early results, we are not remotely satisfied and 6 expect to build on this momentum through the remainder 7 of this year and beyond. We ended the first quarter 8 with 2800 patients on LUMRYZ, reflecting 100 percent 9 growth over the same period last year. Additionally, 10 we re-accelerated the growth of net new patients 11 during Q1, delivering an increase of 300 patients, 12 which is a 50 percent increase compared to the fourth 13 quarter of 2024. 14 Lastly, despite the typical Q1 seasonality 15 headwinds, we generated \$52.5 million in net revenue, 16 which represented greater than 90 percent growth 17 versus Q1 of 2024. 18 Our commercial performance underscores the 19 strong clinical value proposition of LUMRYZ and its 20 unmatched advantage as a once-at-bedtime oxybate. 21 Given the positive momentum year to date, we are 22 raising our revenue guidance to \$255 to \$265 million 23 for the full year. Tom will provide additional 24 details related to this later in the call. 25 As you may recall, effective January 1st, we	1 expansion of our nursing support team, which also 2 doubled in size effective January 1st. This is our 3 team who is directly engaging with patients prior to, 4 at the start of, and during their LUMRYZ treatment. In Q1, 5 we saw an improvement in persistency, or in other 6 words, a decrease in our discontinuation rate when 7 compared to Q4. Importantly, that improvement 8 occurred across all patient segments, including new- 9 to-oxybate patients and in particular during the first 10 90 days of treatment. 11 This positive impact is a result of both the 12 expansion of the team and the implemented training 13 that is designed to both assist patients getting onto 14 therapy and also provide ongoing support during their 15 LUMRYZ treatment. The cumulative impact of these 16 positive trends has resulted in a re-acceleration in 17 the growth of the most important patient metric, which 18 is net new patient adds where we delivered 50 percent 19 growth in Q1 versus Q4. 20 Furthermore, the additions of our new 21 commercial leaders in sales and patient services have 22 been positive catalysts to our recent performance. We 23 expect this will be further enhanced by the impending 24 appointment of our next executive commercial leader. 25 From a timing perspective, we are in the very final
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1 increased our sales force by 15 percent, expanding our 2 target focus and our sales team capabilities. The 3 execution of this and related initiatives resulted in 4 positive patient demand growth across all patient 5 segments during Q1 versus Q4, including growth in 6 switch patients, starts, and an expansion of our 7 LUMRYZ prescriber base. 8 We are encouraged by the continued expansion 9 of new writers who previously, according to currently 10 available data, had not prescribed an oxybate, but who 11 are now beginning to prescribe LUMRYZ. We believe 12 this is another strong data point, highlighting how 13 LUMRYZ is both competing in the oxybate market and 14 growing it. 15 Complementing our sales force, we doubled 16 the size of our field reimbursement team. This 17 expansion, which also took effect January 1st, has 18 rapidly demonstrated the ability to drive additional 19 patient starts faster, while enabling this team to 20 spend more time in the field, directly engaging with 21 targeted prescribers and their office staff, all of 22 which has resulted in an improvement in new patient 23 starts across all patient segments in Q1 when compared 24 to Q4. 25 And lastly, we turn our attention to the	1 stages of this process and expect to announce the 2 appointment of a highly accomplished and experienced 3 rare disease leader who we believe will elevate our 4 capabilities and accelerate our performance. 5 Now, moving beyond LUMRYZ's launch in 6 narcolepsy, a few additional updates that are key to 7 Avadel's future growth and value creation. First, 8 enrollment is progressing and on track in our Phase 3 9 revitalized trial evaluating LUMRYZ in idiopathic 10 hypersomnia. As previously communicated, we expect to 11 complete enrollment in the trial before the end of 12 2025 and are targeting top line data in the first part 13 of 2026, followed by an NDA filing thereafter. 14 To give you a sense of the size of the IH 15 opportunity, there are approximately 42,000 patients 16 diagnosed and only one FDA approved treatment 17 available today, which has reached approximately 10 18 percent of that population. If approved for use in 19 IH, we believe LUMRYZ has the potential to unlock a 20 significant additional unrealized market opportunity. 21 Prescribers regularly express their 22 excitement about the future prospect of being able to 23 prescribe LUMRYZ for indications beyond narcolepsy, 24 and specifically IH. 25 We consistently hear that having an

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1 uninterrupted, predictable, consistent, and fully 2 prescribed oxybate dose night after night is important 3 to patients and physicians. LUMRYZ currently offers 4 that potential for narcolepsy patients who have 5 difficulty staying awake and believe it is only an 6 intuitive to extend that potential possibility to IH 7 patients, who struggle with waking up. 8 With clear market potential and vocal 9 community support, we believe LUMRYZ, if approved, is 10 well-positioned to potentially transform the IH 11 patient experience. Beyond LUMRYZ, we are advancing 12 efforts around a once nightly no or low sodium oxybate 13 program aligned with the target product profile that 14 is bioequivalent to LUMRYZ. We believe this 15 alternative formulation could serve as an additional 16 compelling treatment option to serve patients dealing 17 with hypersomnia related disorders, who could also 18 benefit from the opportunity of an uninterrupted, 19 predictable, consistent, and fully prescribed oxybate 20 treatment night after night. 21 Now, moving briefly on to our litigation, we 22 remain confident in our comprehensive legal strategy. 23 And while we're waiting for decisions on certain prior 24 matters, we are actively pursuing the following 25 actions against Jazz to protect and further build our	1 to walk through our financial results. 2 MR. MCHUGH: Thanks, Greg. Before I begin, 3 please note that full financial results are available 4 in the press release issued this morning and the 10Q. 5 I will also be reviewing non-GAAP financial results, 6 which can be found on our Investor Relations website 7 at investors.avadel.com. 8 Looking at the momentum in patient demand as 9 we closed out Q1 and continued progression through the 10 first month of Q1, we raised our guidance to 11 appropriately reflect our performance expectations for 12 the remainder of 2025. 13 As Greg noted earlier, we raised our full 14 year 2025 net revenue guidance to 255 to 265 million 15 from 240 to 260 million. We also are raising our 16 guidance for patients on therapy to 34- to 3600 17 patients by year end, from 3300 to 3500 patients in 18 prior guidance. And while we are increasing revenue 19 guidance, we are maintaining our previous full year 20 cash operating expense guidance of 180 to 200 million. 21 At this time, given the long term and 22 unknown implications of industry wide changes around 23 potential tariffs and policies impacting biotech, we 24 want to also provide visibility into our near-term 25 expectations for Q2 performance. In that regard, we
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1 business: 2 First, our ongoing defense in the initial 3 patent lawsuit where, as noted, we won an important 4 appeal yesterday. Next, the antitrust case against 5 Jazz, currently scheduled for a jury trial in early 6 November, in which we are seeking total potential 7 recovery well in excess of a billion dollars. And 8 finally, our recently initiated offensive patent suits, 9 in which we are asserting the once nightly use of their 10 mixed salts product in IH, as described in its label, 11 infringes five Avadel patents and which reflects our 12 unwavering commitment to protect our intellectual 13 property. 14 Wrapping up my opening remarks, we are 15 encouraged by the progress made across all aspects of 16 our business, and in particular, the re-acceleration 17 of our LUMRYZ narcolepsy franchise and yesterday's 18 court decision. We remain focused on sustaining this 19 momentum as we continue working toward a long term 20 goal of a billion dollars in LUMRYZ narcolepsy revenue, 21 while expanding our impact to potential patient 22 populations in the future, who may also benefit from 23 a once at bedtime LUMRYZ, leveraging our innovative 24 technology platform. 25 With that, let me turn the call over to Tom	1 expect to generate 60 to 63 million in net revenue 2 during the second quarter of 2025, with cash operating 3 expenses in the range of 45 to 50 million. 4 And by providing this additional guidance 5 during today's call, we hope to impart more certainty 6 and confidence in our full year guidance as we close 7 out the first half of the year. 8 Overall, our increased guidance underscores 9 our conviction in the commercial investments we made 10 at the beginning of this year, what they were designed 11 to achieve, while further confirming that LUMRYZ is on 12 its way to achieving a billion in revenue. 13 Turning to financial updates, in the quarter 14 ended March 31st, 2025, we reported net revenue of 15 52.5 million and gross profit of 46.9 million, 16 compared to net revenue and gross profit in the prior 17 year quarter of 27.2 million and 25.7 million, 18 respectively. 19 Additionally, I'll note that gross profit in 20 the current year includes an adjustment in cost of 21 goods sold for a potential 3.5 percent royalty on 22 LUMRYZ net revenue related to the Delaware Court 23 memorandum and opinion issued in September of 2024. 24 But to be clear, while this matter is pending a final 25 resolution, it is a non-cash expense. A ruling from

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1 the Delaware Court regarding a future ongoing royalty 2 rate is pending, and while we intend to appeal the 3 underlying jury decision regarding the validity of the 4 patent, from an accounting standpoint, we have 5 included a non-cash accrual and cost of goods sold. 6 Also worth highlighting, as we scale above 7 and beyond the \$50 million quarterly revenue level, we 8 expect incremental revenue and patient additions to 9 increasingly flow through to the bottom line. This 10 marks the beginning of a period of financial leverage 11 for Avadel, and moving forward, we expect the growth 12 in revenue and cash flow to continue over the coming 13 year while maintaining financial discipline with 14 regard to operating expenses. 15 Turning to operating expenses, while we 16 reported a 93 percent increase in year over year net 17 revenue, we reported a 3 percent decrease in total 18 operating expenses. Total GAAP operating expenses for 19 the first quarter were 49.9 million, versus 51.7 20 million in the prior year. The current quarter 21 includes 5 million of non-cash charges comprised of 22 stock-based compensation of \$4.2 million and 23 depreciation and amortization of 800,000. 24 After adjusting for these items, cash 25 operating expenses for the quarter were 44.9 million.	1 of 20 to 40 million. 2 And on a final note, we want to address a 3 topic that is top of mind for many: tariffs. As some 4 of you may have heard from our public comments over 5 the last month, based on what we know today, Avadel 6 currently does not expect to be materially impacted by 7 recent trade policy developments as we've taken steps 8 over the past four years to ensure all aspects of our 9 manufacturing, which in turn builds strategic and de- 10 risking redundancies into our supply chain. 11 Importantly, we source our API from two 12 suppliers, both in the United States, and this has 13 resulted in the majority of our manufacturing now 14 being based in the U.S. And in addition to sourcing 15 all API in the U.S., our U.S.-based manufacturer is 16 already FDA approved and is fully operational. With 17 that said, we have the ability, if needed, to source 18 exclusively from our U.S. domestic partners. 19 With that, I'll turn the call back to Greg 20 for closing remarks. 21 MR. DIVIS: Thank you, Tom. 22 Before we open the call for Q&A, let me 23 summarize the opportunities that we believe can unlock 24 value for Avadel in 2025 and beyond. First, our 25 commercial investments have accelerated our growth and
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1 The leverage inherent in our operating model is 2 increasingly evident as incremental revenue and 3 patient additions continue translating effectively 4 into improved cash flow and profitability. We view 5 this as a key inflection point and a validation of the 6 strategic investments we've made during our initial 7 launch phase. 8 With respect to cash, the company ended the 9 first quarter with 66.5 million of cash, cash 10 equivalents, and marketable securities. We also want 11 to take the opportunity during this call to provide 12 perspective on our path to achieving sustainable 13 operating breakeven and cash flow. 14 During the first quarter, GAAP operating 15 loss was 3 million. After adjusting for non-cash 16 operating expenses, adjusted operating income was a 17 positive 2 million, calculated as gross profit of 46.9 18 million minus cash operating expenses of 44.9 million. 19 This marks the third consecutive quarter of positive 20 adjusted operating income for the company. 21 And while cash flow was negative in the 22 first quarter due to working capital requirements and 23 higher gross nets, we expect cash flow for the full 24 year, based on current plans and assumptions, to be in 25 the range of 30 to 40 million versus previous guidance	1 further advanced our growing leadership position in 2 the narcolepsy community. We achieved strong results 3 during the first quarter and expect continued 4 execution during the remainder of this year. 5 We are well positioned to generate 6 sustainable, positive cash flow from the trends we are 7 seeing, which is further bolstered by our highly 8 leverageable cost structure and our increase in 2025 9 revenue guidance. We're pursuing opportunities to 10 maximize potential of our unique once-at-bedtime 11 formulation beyond narcolepsy through our lifecycle 12 management initiatives, and are confident in our 13 team's expertise to turn the promise of our innovative 14 science into reality that could possibly benefit even 15 more eligible patients. 16 Based on our successful past actions to 17 diversify and de-risk our supply chain, we are well- 18 positioned relative to the current tariff dialogue, as 19 our infrastructure is predominantly based in the U.S., 20 and we currently anticipate little to no impact. 21 And finally, underpinning our progress lies 22 our robust and growing intellectual property portfolio 23 that protects LUMRYZ and its underlying innovation 24 until 2042. This is a foundational strength that we 25 will continue to protect and defend, which is

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1 representative in our recent actions in this regard. 2 As always, we thank you for your time and 3 your support and joining us today, and will now open 4 the line for Q&A. Operator. 5 6 OPERATOR: Thank you. As a reminder to ask 7 a question, you will need to press *11 on your 8 telephone. To remove yourself from the queue, you may 9 press *11 again. Please stand by while we compile the 10 Q&A roster. 11 Our first question comes from the line of 12 Marc Goodman of Leerink. Please go ahead, Marc. 13 Marc, your line is open. Please make sure your line is 14 unmuted. And if you're on a speakerphone, lift your 15 handset. 16 Go to the next question, which comes from 17 the line of Andrew Tsai of Jefferies. Your question 18 please, Andrew. 19 MR. TSAI: Hey. Good morning. Thanks for 20 taking the questions. Congrats on the nice progress. 21 My first question is around the revised 2025 guidance. 22 At the midpoints around 260, you did 52.5 in Q1. 23 You're guiding to 61.5 at the midpoint for Q2. So 24 about 115 million for first half 2025. 25 So is it fair to assume to get to your	1 So I can correlate the expansion of our 2 sales team and the expansion of our -- and switch and 3 some modifications to our commercial execution that 4 have driven, you know, more demand at the top of the 5 funnel. Our expansion of our field reimbursement team 6 certainly has pulled through patients faster to get 7 more patient starts. And then, you know, the early 8 signs of our work on persistency certainly has trended 9 very well to start the year. 10 I think in all cases, we expected to see 11 most of that improvement to begin to kick in in Q2 and 12 beyond as we were getting our teams up and running. 13 So we're pleased that we've jumped off pretty fast 14 from that perspective and have continued that momentum 15 here in the first month of Q2. 16 So we're excited about those prospects, and 17 I think all aspects of it are advancing in the right 18 direction. And, you know, but recognizing we've got a 19 lot more to accomplish and a lot more to deliver. 20 MR. TSAI: Right. Makes sense. And then, 21 secondly, congrats on winning the appeal case 22 yesterday. Was the precise nature of that ruling 23 aligned with your base case scenario, or was that 24 perhaps the best case scenario for you? And then 25 where do we go from here? When would be the next
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1 guidance, sales should be growing at a similar pace in 2 Q3 and Q4, or could there be bumpiness along the way? 3 And if you had to rank order all the reasons why 4 you're growing, such as improved gross and net less 5 dropouts, more patient adds, what would that growth be 6 based on exactly? Thank you. 7 MR. MCHUGH: Hey Andrew, it's Tom. Thanks 8 for the question. Yeah, you're exactly right. The 9 first half of the year, at the midpoint of the 10 guidance, you know, it's about 114 million in the 11 first half of the year, which obviously leads to 12 plenty of growth in the second half of the year. 13 You know, in terms of your question around 14 sequence or sort of the cadence of quarterly net 15 revenue, our goal is always is to grow quarter over 16 quarter and with, you know, leaving plenty of room to 17 grow in the second half of the year, we would expect 18 sequential growth quarter over quarter for the 19 remainder of the year. 20 MR. DIVIS: Yeah. Andrew, this is Greg. 21 Thanks. In terms of your second question about like 22 what are the drivers and, you know, can we pinpoint or 23 point to the major initiatives that have driven some 24 of the improvements, I think, you know, in short, 25 we've seen every key metric improve versus Q4.	1 quote/unquote litigation update? Is it basically when 2 or if LUMRYZ is approved in IH later in 2027? 3 MR. DIVIS: Yeah, I think the short answer 4 is that was our base case assumption. And we're 5 pleased with the results that came out as it's a clear 6 and favorable and critical decision for us and for 7 patients, so, you know, given the fed circuit 8 overturned some key aspects, important parts of that 9 injunction. 10 In terms of what's next in that regard, you 11 know, that will be, you know, dependent upon others 12 from that perspective. For us, it just gives us the 13 clear path to continue to execute our plans that we 14 had been planning to execute and advancing toward an 15 NDA submission in IH as we complete the trial from 16 that standpoint. So we're pleased with that decision 17 and look forward to continue moving forward. 18 MR. TSAI: Great. Thanks again. Congrats. 19 OPERATOR: Thank you. Our next question 20 comes from the line of David Amsellem of Piper 21 Sandler. Please go ahead, David. 22 MR. AMSELLEM: Thanks. So just a couple for 23 me. You know, with IH, your competitor announced 24 patient metrics last night for their product. And I'm 25 just wondering, how are you thinking about the patient

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1 footprint, potential patient footprint for LUMRYZ in 2 IH? Do you think it'll look similar to what we've 3 seen for your competitor? That's number one. 4 And then number two, just taking a step 5 back, being a single product company, certainly, you 6 know, has its pitfalls, particularly in this macro 7 environment. I guess my question is, you know, the 8 success of LUMRYZ, notwithstanding, what's your 9 appetite for bringing in another asset or assets to 10 further drive growth of the company? Thanks. 11 MR. DIVIS: Yeah. You know, to your first 12 question on how we view the IH opportunity, we view it 13 as highly untapped and ripe for, you know, new 14 treatment options that offer our own unique and 15 differentiated clinical value proposition. And we 16 believe from that standpoint, like we've seen with 17 narcolepsy, we can be successful sourcing patients 18 from all segments, right? Patients who are diagnosed 19 and not being treated today with an oxybate, patients 20 who may want to or who struggle with waking up in the 21 middle of the night to take a treatment that for a 22 condition where, you know, deep sleep inertia makes it 23 very challenging or for, you know, you know, new 24 patients who are coming into the fold, so to speak. 25 So we believe it's ripe for all those -- all	1 or programs to our portfolio that is strategic and 2 aligned with what we're doing today. And that's key. 3 But from that perspective, our priorities are as I've 4 just laid out. 5 MR. AMSELLEM: Thank you. 6 MR. DIVIS: Thanks, David. 7 OPERATOR: Thank you. Our next question 8 comes from the line of Marc Goodman of Leerink. 9 Please go ahead, Marc. 10 MR. GOODMAN: Hey, guys. Sorry about that 11 before. Tom, can you give us a sense of the average 12 selling price in the quarter and how you're thinking 13 about that for the rest of the year? Have there been 14 any changes with respect to in the guidance and stuff? 15 Thanks. 16 MR. MCHUGH: Yeah. Marc, thanks for the 17 question. You know, you know, just as a reminder, Q1 18 is always heavily impacted by gross net. And if you 19 just work through the math of our net revenue and 20 average patients on therapy, you know, average net 21 revenue for all patients, including patients on free 22 drug, average, you know, a little under \$80,000 23 annualized. But again with the reminder that Q1 is 24 always impacted by gross nets, our expectation is that 25 net revenue is going to improve throughout the year.
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1 those positions, all those opportunities. And LUMRYZ 2 is well-positioned in that regard for this patient 3 population, as we've heard, you know, extensively time 4 and time again from physicians and patients alike who 5 are looking for a treatment option, where you can get 6 the consistent, predictable, full therapeutic 7 treatment night after night. And that's what LUMRYZ 8 offers. 9 In terms of your comment or question about 10 IH, about, you know, kind of as a single product 11 asset, we view it as a pipeline in a -- in a program 12 from that perspective. We believe there's multiple 13 shots on goal to leverage the innovative technology 14 that we've developed with LUMRYZ and our platform to 15 potentially, you know, benefit more patients who are 16 pursued through life cycle management and other 17 related initiatives. 18 So when you think about, you know, capital 19 allocation and what's most important, you know, 20 focusing on the launch, deploying our capital to drive 21 the commercial execution and launch of LUMRYZ is 22 number one, and executing these initiatives from a 23 life cycle management is number two, for sure. 24 It doesn't mean we don't have -- we wouldn't 25 be in the appetite or have the appetite to add assets	1 MR. GOODMAN: And so for the full year, 2 you're expecting it to be what? Last year was around 3 96,000. What are you thinking this year? 4 MR. MCHUGH: Yeah, listen, it's hard to 5 predict the full year, Marc. Maybe I'll just 6 reference last year as an example. You know, from Q1 7 to Q2, we saw an improvement in net revenue per 8 patient of about 5 percent from Q1 to Q2. You know, I 9 think that we're looking right now, based on what we 10 see today, the same sort of improvement from Q1 to Q2 11 of this year. But again, you know, the full year is 12 always hard to predict, but we're expecting 13 improvement in net revenue, certainly for the full 14 year versus what we saw in Q1. 15 MR. DIVIS: Yeah. And I think that a major 16 driver of that over time, Marc, will be more patients 17 on therapy longer at steady doses relative to the 18 number of new starts, which obviously started at a 19 lower value from that perspective. 20 MR. GOODMAN: Thanks. 21 OPERATOR: Thank you. Our next question 22 comes from the line of David Huang of Deutsche Bank. 23 Please go ahead, David. 24 MR. HUANG: Hi. Thanks so much for taking 25 the questions and congrats on the quarter. So just a

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1 couple on, I guess, kind of what you're seeing in 2 terms of the patient mix. 3 So did you get, I guess, a better mix of 4 switch versus new to oxybate patients this quarter? I 5 seem to remember, you know, last quarter you talked 6 about moving it in a more favorable direction. 7 And then can you just talk a little bit 8 about the tactics which were used to improve 9 persistency, especially among the new to oxybate 10 patients, and whether you think there's room to 11 further improve persistency? Thank you. 12 MR. DIVIS: Thanks, David. On your first 13 question about mix, I think most importantly, we saw 14 every patient segment improve in Q1 versus Q4 with an 15 acceleration in switch patients from that standpoint. 16 So we did see on a percentage basis, we saw an 17 improvement in switch as an overall relative to our 18 patient starts in Q1. 19 So we're pleased with that progress. 20 That's, in large part, driven by, you know, our 21 commercial execution and both the combination of 22 expanding our reach and how we've layered in some 23 additional initiatives and focus for our organization 24 to really drive that demand across the entire universe 25 of potential prescribers, which is where we saw a lot	1 possible, but we thought was more unlikely, and we 2 thought we'd start seeing that impact later this year. 3 But we've seen it from the get-go. And again, that 4 has continued through the first month of Q2. 5 MR. MCHUGH: Yeah, maybe I'll just add to 6 that, you know, persistency and, you know, switch 7 patients are important from a revenue perspective, 8 certainly. But really, all patients are important to 9 us. And you know, as I commented during the prepared 10 remarks, I would characterize we sort of reached that 11 critical mass of patients on therapy where every 12 patient that's added at this point is a drop to the 13 bottom line for us. 14 OPERATOR: Thank you. Our next question 15 comes from the line of Maryam Bagheri of LSC. Please 16 go ahead, Maryam. 17 MS. BAGHERI: Hello and congrats on the 18 quarter. Thank you for taking my question. Just on 19 the news from yesterday, it sounded like the federal 20 court kind of remanded to the district, to the 21 district court reconsideration on the patent 22 infringement issue. Could you just explain what that 23 entails exactly and whether an injunction is still 24 possible, just given the news there? 25 MR. DIVIS: Yeah. What, you know, without
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1 of growth coming in Q1 from physicians, who I would 2 say have prescribed or marginally prescribed, but not 3 consistently prescribed, or hadn't prescribed at all. 4 We saw a lot of improvement in that area as a function 5 of us expanding our reach from that perspective. 6 In terms of your question around 7 persistency-related matters, I think most important 8 what we've done is we've expanded our nurses so their 9 caseload can really allow them to have a more in-depth 10 kind of engagement with the patient, not only at the 11 beginning of the process, but all the way through the 12 process. 13 And as a result of that, we've implemented a 14 number of initiatives in terms of at-initiation of 15 treatment and post-initiation of treatment to continue 16 to engage the patient regularly, in particular, during 17 these first kind of 90 days. 18 And again, you know, by no stretch do I 19 think we've gotten to the floor. I think there's 20 opportunities to continue to do better and our 21 programs and initiatives operating at even a more 22 efficient and effective level. 23 But we're really pleased to see that as 24 early as Q1, we saw, you know, a trend going the other 25 direction, which was something that we thought was	1 trying to get, you know, you know, play attorney from 2 that perspective in totality on this matter where the, 3 you know, the federal circuit, you know, vacated, you 4 know, the notion of enjoining us from seeking 5 approval. 6 What the district court -- or what the -- 7 what the fed circuit basically said is they're sending 8 it back to the district court on the basis that the 9 analysis that the district court had in making that in 10 joint -- enjoining us on seeking an approval was too 11 speculative and tenuous to reasonably conclude that, 12 you know, enjoining Avadel from applying for FDA 13 approval is necessary to prevent future infringement. 14 Right. 15 So what, in essence, the fed circuit did is 16 they remanded it back to the district court to 17 consider that, you know, in the future from our 18 perspective. Right. 19 But for us, it's very clear and very 20 straightforward that that vacatur gives us a pathway to 21 file and secure and seek FDA approval. And that is 22 the very important next step in our strategy here to 23 be able to pursue that. 24 Because I'll remind everybody 24 hours ago, 25 we were enjoined from doing that and now we're not.

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1 Right. Which is really, really important from that 2 perspective for us as we think about our strategy to 3 advance LUMRYZ in IH or even other potential 4 indications as we -- as we do that work. This is an 5 important win for us, and we're very pleased with the 6 outcome. 7 MS. BAGHERI: Makes sense. Congratulations 8 on that win. Thank you. 9 OPERATOR: Thank you. Our next question 10 comes from the line of Ash Verma of UBS. Please go 11 ahead. Ash. 12 MS. VERMA: Hey. Good morning. This is on 13 behalf of Ash. Congrats on the news yesterday. So I 14 have a two and a follow up question, if I may. So the 15 first one for the IH. How -- I guess how confident 16 are you that your competitor may not attempt to block 17 you with another preliminary injunction when you 18 ultimately try to seek the FDA approval? 19 And the second one on the LUMRYZ patient 20 mix. Do you have any specific goal for where you want 21 the split to be in terms of like a naive versus a 22 switch patients? Like, how are you tracking towards 23 that goal? And I have a follow-up after that. 24 Thanks. 25 MR. DIVIS: Yeah. So I'll take the first	1 in other indications like IH to the same lens from 2 that perspective. And we believe the opportunity to 3 bring LUMRYZ to those patients is really, really 4 important. 5 What anyone else tries to do, they'll do 6 from that perspective. We'll be prepared for it. And 7 we have, we believe, a track record that shows that we 8 can be successful. 9 MR. MCHUGH: Yeah. With regard to your 10 question on patient mix, you know, again, we're really 11 pleased with the results we saw in Q1, including one 12 of the metrics, which was an improvement in the 13 percentage of our patients who started therapy and 14 remained on therapy that were switch patients. You 15 know, that was off from Q4 going into Q1. 16 But, you know, just a reminder, the oxybate 17 market is a large market, and we're focused on growing 18 all patient segments, whether it be switch patients or 19 new to oxybate patients or return to oxybate patients. 20 And for us, as I commented just a few 21 minutes ago, you know, we have reached that critical 22 mass of patients on therapy where patient growth, 23 regardless of which patient segment, is going to 24 contribute to our profitability and our cash flow. 25 MR. DIVIS: I think it's a really important
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1 part of the question and then we can certainly -- Tom 2 can comment on mix a little bit. 3 I think it's really important to, again, 4 remind everyone that, you know, well, first of all, I 5 won't speak for what other parties may or may not do. 6 That's not for me to predict or, you know, provide 7 commentary on what others may do. It's our -- it's 8 our responsibility to be prepared for any situation 9 that can occur, which I can assure you, we have been 10 and, you know, there's been a lot of historical 11 commentary that we would be denied from getting an 12 approval in narcolepsy. We would be blocked from 13 getting orphan exclusivity. 14 All of those things occurred. And I'll 15 remind you that we have -- we got an approval with 16 orphan drug exclusivity in narcolepsy twice for adults 17 and for pediatrics, and that was confirmed by a 18 district court from that standpoint. 19 So the district court, along with the FDA, 20 has a clear understanding of the clinical superiority 21 and differentiation of LUMRYZ in narcolepsy, and it 22 was recognized that the public interest would be 23 served having that -- our superior drug available for 24 people with narcolepsy. Right? 25 We're prepared to continue to develop LUMRYZ	1 comment that I'm just going to reemphasize that our 2 source of patients, we're not relegated to only 3 seeking patients from new to oxybate patients. We're 4 not only competing in the 3- or 4000, 5000 patients 5 who are coming in every year to get new to oxybate -- 6 as a new to oxybate patient. 7 Although we're getting our -- we're getting 8 patients in that segment, we're sourcing patients from 9 switch and previously treated who are returning to 10 oxybate. And that pool is, you know, multiple times 11 larger than that of the new to oxybate patients. So 12 we're confident in our prospects to continue to grow 13 and to continue to build LUMRYZ. 14 MS. VERMA: Thanks for that. Just a follow 15 up like wanted to understand more on the 2026 16 implications for narcolepsy market pricing, just based 17 on the potential variable generic entry. Can you 18 share your latest thoughts on that? And is setting up 19 the ramps cost prohibitive for generics? And thus you 20 see a very low chance of that happening? Thanks. 21 MR. DIVIS: Yeah. Thanks. I would say our 22 overall kind of macro view on the potential for 23 additional generics in 2026, much like what we've seen 24 with the current authorized generic is it has had very 25 little, if at all, impact on pricing or opportunity

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1 and formulary positioning and uptake for any branded 2 oxybate in that -- for that matter, and in particular 3 in our case, LUMRYZ. 4 So I think we have to be prepared, and I 5 can't comment as to whether or not the wherewithal of 6 potential generic suppliers will or won't, you know, 7 invest in a REMS. They're going to have to. If they 8 want to be in it, they're going to have to invest in 9 it, and they're going to have to manage it 10 accordingly. 11 But we do -- we have done a lot of work in 12 this regard in dealing with our payers, and what we 13 can expect could potentially be the net impact of 14 this, if it does come, and pricing does collapse for 15 the, you know, relatively speaking, for the multi- 16 source generics in this case. 17 And our view is that where they're likely to 18 be positioned is going to be in the case for, if you 19 will, new to oxybate patients. 20 So in that case, if they are positioned as 21 in some cases a step edit for new to oxybate patients 22 have to fail at twice nightly generic, if you will, 23 from that standpoint, we think we're -- we think we're 24 very well-positioned to capture the switch patient 25 coming off of that start, in particular under the, our	1 updated guidance for the year? 2 MR. DIVIS: Yeah. 3 MS. FADIA: And I have one or two other 4 questions. 5 MR. DIVIS: Yeah. Thanks, Ami. I think the 6 best way to think about how we think about and to 7 share with you how we think about the improvements in 8 discontinuations or our lack -- or a decline in those 9 or -- and/or the improvement in persistency is when 10 you look at how we think about those rates inside 11 of -- inside of a quarter, in Q4, we had calculated 12 that discontinuation rate to be about 14 percent. 13 And in Q1, although we had assumed that 14 maybe that would stay flat or tick up in Q1 because of 15 our patient mix in Q4, we saw that number go down. So 16 our number is lower than 14 percent. And we saw that 17 occur across all patient types with the most 18 pronounced impact on new to oxybates and in particular 19 in the first 90 days. 20 So our expectation is that we should 21 continue to see some improvement in that regard as we 22 continue to move forward in our systems and our 23 programs get even more effective from that 24 perspective. It will never get to zero, but we will 25 continue to drive it as low as we can get from that
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1 view, that the investments that we have to make and, 2 you know, other companies have made to try to help 3 patients stay on therapy is high, and it costs a lot 4 of money. 5 I'm not sure that that every generic company 6 will do that. But from our perspective, we think 7 we're well-positioned to continue to grow LUMRYZ in 8 the face of more generics in particular. Like I just 9 said, the largest segment we're getting patients from 10 are switch and previously returned, previously treated 11 and discontinued. And we're well-positioned to 12 continue to get those as well as any step through 13 to -- from a new to oxybate patient. 14 MS. VERMA: Great. Thank you and congrats 15 again. 16 OPERATOR: Thank you. Our next question 17 comes from the line of Ami Fadia of Needham. Please 18 go ahead, Ami. 19 MS. FADIA: Good morning. Thanks for taking 20 my question. It's nice to see the progress that's 21 been made in the quarter with all the changes that you 22 made effective early in the year. Can you give us 23 some color on and maybe any specifics you can share 24 around the discontinuation rates, how they have 25 evolved, and what assumptions you've made in your	1 standpoint. 2 MR. MCHUGH: Yeah. And Ami, on your 3 question regarding, I'll say, implications to guidance 4 on the improvements in persistency, is it part of 5 the reason we raised the guidance. You know, we have, 6 you know, certainly increasing levels of confidence 7 and conviction in the programs we put in place. Our 8 goal is to continue to move forward and continue to 9 improve. 10 And, you know, to state the obvious, the 11 longer we keep patients on therapy, you know, the 12 higher revenue is going to be. So it's an important 13 initiative for us. And again, we're just very pleased 14 with what we saw in Q1 and what we're seeing for 15 continuing trends in the very, very early part of Q2. 16 MS. FADIA: Got it. Can you also talk about 17 some of the sort of offensive lawsuits that you 18 highlighted in your prepared remarks in IH? Can you 19 elaborate on that? It sounds like that's a new 20 lawsuit. 21 And then with regards to the federal court 22 decision that was sent back to the district court, can 23 you talk about the timelines around next steps there? 24 MR. DIVIS: Yeah. On your -- on your first 25 question around the other suits that we have filed,

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1 this is us just asserting our innovation and our -- 2 and our, you know, that we've -- that we've developed 3 in the form of LUMRYZ and related formulations and 4 products for hypersomnia related disorders. 5 And so we have taken our own actions against 6 Jazz in this regard, in that in our view that their 7 label and their IH label specifically around once 8 nightly dosing for a small percentage of their 9 patients infringes our intellectual property. 10 So it's very straightforward from that 11 perspective. We have five patents that have been 12 allowed and granted that we believe they're 13 infringing. And so we've asserted our right, as we 14 have the right to do from that perspective. 15 Again, I think as it relates to the 16 decisions that came out of the court yesterday, I 17 think most important from that standpoint is that 18 we're obviously pleased with that decision. Right. 19 We're pleased. We think it's a clear, concise, 20 straightforward and important win for us. 21 In terms of what happens next, there is, I 22 would just say, administrative, you know, steps that 23 have to occur. Parties need to meet and confer. 24 There's the Delaware Court has set a timeline to 25 report back to them by. I think it's May. In May	1 Chase. 2 MR. KNICKERBOCKER: Good morning. Yeah. 3 Congrats on the nice results here. I'll share mine as 4 well. Just first from me, as we await some data on 5 the Orexin agonist this year, can you just remind us 6 on how you see the market fleshing out over the next 7 couple of years as it relates to NMEs and these, you 8 know, how you see the competitive environment, how you 9 see, you know, kind of the split of the market, how 10 these drugs can work together, et cetera? 11 MR. DIVIS: Yeah. I think, you know, first 12 and foremost, you know, we, like everyone, are paying 13 close attention to this and following it accordingly. 14 And there's clearly a lot of investor enthusiasm about 15 their prospects. But for us, what we're most 16 interested in is the clinicians and our prescriber 17 perspective. 18 So I would -- and we've done a lot of work 19 in this regard. We've come up -- come off of a fairly 20 large recent comprehensive research project, talking 21 to both key opinion leaders and a broad base of sleep 22 expert -- sleep specialists who treat a lot of these 23 patients. And there's certainly excitement about this 24 mechanism of action because of the nature of their 25 wakefulness or wake promoting prospects.
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1 22nd. So there's things that are going to begin to 2 occur between both parties from that perspective. But 3 at the end of the day, we're very pleased with this 4 decision to put us in a pathway to go forward. 5 MR. MCHUGH: Thanks, Ami. 6 MS. FADIA: Got it. Maybe if I can squeeze 7 in one quick question. Is that okay? 8 MR. MCHUGH: Sure. 9 MS. FADIA: Okay, great. Just with regards 10 to the low sodium once nightly formulation, you've 11 continued to sort of work on that. Any specific color 12 or time frame you can put on that, that would be 13 helpful. Thank you. 14 MR. DIVIS: No, I think our expectation is 15 we'll have -- we'll have more to say this year in this 16 regard based on the work we've -- and, you know, the 17 efforts our team has deployed during the first part of 18 this year and where we think that that's an important 19 step for us as well. And we'll look forward to 20 providing updates in the future on it. Thanks, Ami. 21 MS. FADIA: Thank you. 22 OPERATOR: Thank you. Once again, to ask a 23 question, please press *11 on your telephone. Our 24 next question comes from the line of Chase 25 Knickerbocker of Craig-Hallum. Please go ahead,	1 I think there's less clear view in terms of 2 what impacts they may have on the nighttime. And what 3 physicians tell us very clearly is that, you know, 4 narcolepsy and these disorders are both daytime and 5 nighttime conditions from that standpoint. 6 And so the view we get that, you know, 7 should, you know, the erections navigate all the 8 different regulatory and clinical and regulatory- 9 related matters that they have to navigate to get to a 10 final and full approval at some point in the future, 11 the feedback we receive from physicians is they 12 certainly see an important role for oxybates, in 13 particular, because of its benefit in the night time 14 and the opportunity for that to have complementary 15 benefit to the daytime. 16 But when you think about the disrupted 17 nighttime sleep, hallucinations, sleep paralysis, 18 these things are important to be considered. And 19 oxybates are the standard of care in that regard. 20 So we're quite bullish on the prospects of 21 LUMRYZ and the oxybate category in a post-erection 22 world from that standpoint. And it's something we'll 23 continue to stay close to as we -- as their 24 development programs continue to move forward. 25 MR. MCHUGH: Hey Chase, it's Tom. Maybe

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1 I'll just add to that. You know, it's very exciting 2 technology and the investor community is obviously 3 very interested in Orexins, but it's a long road, 4 right, you know, from going from a controlled clinical 5 setting to an FDA approval and ultimately to 6 commercialization. It's a long path and sometimes 7 difficult path. And we're probably, you know, two to 8 three years away from seeing Orexins come on the 9 market. If they -- if they do get through the 10 approval process and commercial launch process. 11 MR. KNICKERBOCKER: Thanks for the thoughts, 12 guys. And then, Tom, maybe one more for you. Thanks 13 for all the comments on the manufacturing side, but 14 just to kind of put a finer point to it. Can you 15 just, you know, as we await kind of the pharma tariffs 16 in the next couple of weeks, can you remind us, let us 17 know kind of how you treat transfer pricing within 18 your organization and whether or not there could be 19 any potential exposure there, depending on how these 20 tariffs are struck? Thanks. 21 MR. MCHUGH: Yeah. Chase, I don't want to 22 venture too far into the theoreticals and 23 hypotheticals on that question. But, you know, we are 24 an Irish-domiciled company. But I want to reiterate 25 the point that, you know, we have Domestic U.S.	1 CERTIFICATE OF TRANSCRIPTION 2 3 Jane Rose Reporting does hereby certify that 4 the foregoing transcript is a true and correct record 5 of the recorded proceedings; that said proceedings was 6 transcribed to the best of our ability from the audio 7 receiving; and that Jane Rose Reporting is neither 8 counsel for, nor related to, any of the parties to 9 this case, and have no interest, financial or 10 otherwise, in its outcome. 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 _____ Jane Rose Reporting May 8, 2025
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1 manufacturing throughout the supply chain that's 2 available to us, which really, you know, mitigates, 3 you know, you know, substantially, if not altogether, 4 the potential impact of tariffs. 5 So I don't really want to get too far into 6 the, you know, the question around transfer pricing, 7 but I feel like we're really well situated right now. 8 And we're prepared for whatever may come down the road 9 with respect to tariffs. 10 MR. KNICKERBOCKER: Thanks, guys. 11 OPERATOR: Thank you. I would now like to 12 turn the conference back to Mr. Divis for closing 13 remarks. Sir. 14 MR. DIVIS: Thank you very much. We 15 appreciate all of you joining us today. And we look 16 forward to providing you additional updates throughout 17 the balance of this year as we continue to make 18 progress. Thank you very much. Have a great day. 19 OPERATOR: This concludes today's conference 20 call. Thank you for participating. You may now 21 disconnect. 22 (End of Audio Recording.) 23 24 25	

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EXHIBIT 7

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IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC.,	)	
Plaintiffs,	)	C.A. No.
v.	)	21-691-GBW
	)	
AVADEL CNS PHARMACEUTICALS, LLC,	)	
Defendant	)	
-----	)	
	)	C.A. No.
JAZZ PHARMACEUTICALS, INC., et al.,	)	21-1138-GBW
Plaintiffs,	)	
v.	)	
	)	
AVADEL CNS PHARMACEUTICALS, LLC,	)	
Defendant.	)	
-----	)	
	)	
JAZZ PHARMACEUTICALS, INC., et al.,	)	
Plaintiffs,	)	C.A. No.
v.	)	21-1594-GBW
	)	
AVADEL CNS PHARMACEUTICALS, LLC,	)	
Defendant.	)	

- - - -
Wilmington, Delaware
Thursday, June 6, 2024
Permanent Injunction Transcript

- - - -
BEFORE: HONORABLE GREGORY B. WILLIAMS
UNITED STATES DISTRICT COURT JUDGE

- - - -
Michele L. Rolfe, RPR, CRR

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22 For Defendant

23 - - - -

24 PROCEEDINGS
25 (REPORTER'S NOTE: The following permanent injunction
hearing was held in Courtroom 6B beginning at 9:00 a.m.)
THE COURT: Good morning. You may be seated.
We're here this morning for the hearing on

1 that's okay with Your Honor. We're going to do the PI
2 first, back and forth if you will, and then we'll move on to
3 the ongoing royalties, the second section.

4 THE COURT: Okay.

5 MR. CERRITO: Second issue was raised was
6 confidentiality, Your Honor. Defendants don't seem to have
7 any issues here, we have quite a bit. I'm not sure which --
8 how Your Honor would proceed here.

9 It's throughout our presentation, it includes
10 very sensitive, competitive information; the type of which
11 we talk about outside this courtroom somebody would say
12 we're colluding and price fixing. So we simply cannot have
13 representatives from Avadel outside the protective order in
14 the courtroom.

15 MS. DURIE: May I be heard?

16 THE COURT: Yes.

17 MS. DURIE: Thank you. Your Honor, we
18 endeavored to meet and confer about this evening and we
19 offered to exchange that information. Jazz refused to meet
20 and confer about it.

21 We have prepared our presentation mindful of
22 confidentiality restrictions. We think that we can make the
23 arguments without the need to say the specifics of the
24 confidential information. It's in the record, the Court can
25 look at it, but there's no reason we need to say it or

1 Jazz's preliminary -- motion for preliminary injunction.
2 Civil Action 21-691. Let's start by having counsel put the
3 appearances on the record.
4 MR. TIGAN: Good morning, Your Honor. Jeremy
5 Tigan with Morris Nichols on behalf of Jazz. I'm joined by
6 my colleagues from Quinn Emanuel today: Nick Cerrito, Frank
7 Calvosa and Gabriel Brier at counsel table.

8 Behind them is Krista Rycroft and Tyler
9 Crudentaria.

10 And our client representative James Sicola is
11 here as well.

12 THE COURT: Good morning.

13 MR. SILVER: Good morning, Your Honor. Dan
14 Silver from McCarter & English on behalf of Avadel. I'm
15 joined by Daralyn Durie and Kira Davis from Morrison
16 Foerster. Ken Schuler and Mark Zubick from Latham &
17 Watkins.

18 And behind the bar, Your Honor, we have Greg
19 Divis, Tom Cue and Craig Simon all from Avadel.

20 THE COURT: All right. Good morning all.

21 MR. CERRITO: Before we begin, Your Honor, a
22 couple of housekeeping matters?

23 THE COURT: Yes.

24 MR. CERRITO: The parties have talked this
25 morning and we've agreed on the presentation order, if

1 publish it.

2 This is a critically important case. This is an
3 existential case for our company, which is why our CEO and
4 our CFO are here. They have an interest in hearing these
5 proceedings. The press is here as well. We think this
6 should be a public hearing. And to the extent that Jazz
7 wants to refer to confidential information, we think they
8 can simply direct the Court to it.

9 In the alternative, if we're going to clear the
10 courtroom, we think we should do that slide-by-slide not for
11 the entirety of the proceedings. The Court may remember
12 Dr. Rainey's testimony at trial, the Court was cleared for
13 the entirety of that testimony and afterwards the Court
14 remarked that there was very little of it that was actually
15 highly confidential.

16 So our view is we should proceed. We think the
17 parties ought to be able to handle it without the need to
18 clear the courtroom, but if they do it should be
19 slide-by-slide, and it should be on their time.

20 MR. CERRITO: Your Honor, I'm happy to show Your
21 Honor the substantial amount of material that I'm talking
22 about. It's not -- back and forth back and forth is going
23 to break up our presentation. We have the burden of proof
24 here. While defendants don't have any confidential
25 information they are worried about, they should, there's

1 internal e-mails from them, internal discussions, pricing
2 issues, rebate issues. It's simply -- I don't know how that
3 we can break it up in a way that is -- that doesn't disrupt
4 the presentation. I'm happy to do a sidebar with Your Honor
5 and show you the materials we're talking about.

6 THE COURT: All right. Yes, let's go to
7 sidebar.

8 (Whereupon, a discussion was held at sidebar as
9 follows:)

10 MR. CERRITO: I just flagged a very short piece
11 of it. These are internal discussions about removing Jazz,
12 basically removing them from insurance companies, kicking
13 Jazz out of the market. So while we're here today, the
14 choice was good and they didn't make a choice --

15 MS. DURIE: So before you move on, I just wanted
16 to address that slide so we can talk about each one.

17 MR. CERRITO: If we're going to talk about each
18 one, we're going to be here all day.

19 MS. DURIE: On that one, that is an e-mail that
20 is an Avadel e-mail, we're fine with having that published.

21 MR. CERRITO: Okay. There's pricing information
22 from PBMs, what discounts we gave them. This is their
23 internal documents. Again, if you don't care...

24 MS. DURIE: For pricing information we do. I
25 think the answer there is the Court can have the information

1 to have to manipulate every sentence that I do in this area.
2 Now, if we want to say "price erosion," the part
3 where this PBM stuff we close the courtroom for that, maybe
4 that's the way to do it.

5 THE COURT: Okay. So maybe -- it sounds like
6 the price erosion and the rebates are really the most
7 sensitive information.

8 MR. CERRITO: Yes.

9 THE COURT: So what if we when we get to that,
10 we clear the courtroom for that.

11 MR. CERRITO: That's acceptable.

12 Understood, Your Honor, I appreciate that.

13 THE COURT: All right.

14 MR. SILVER: Thank you, Your Honor.

15 MS. DURIE: Thank you.

16 (Whereupon, the discussion held at sidebar
17 concluded.)

18 THE COURT: All right. You may approach.

19 MR. CERRITO: May I approach, Your Honor?

20 THE COURT: Yes.

21 MR. CERRITO: Thank you, Your Honor.

22 (Discussion held between counsel off the
23 record.)

24 MS. DURIE: Apparently, they are not willing to
25 provide me with their presentation.

1 in front of it, counsel can just refer to it and Your Honor
2 can look at it and we can make relevant arguments.

3 THE COURT: My concern about just clearing the
4 courtroom for the entire hearing is that, you know, that
5 takes a very high showing and if that was going to be the
6 case, we should have did that ahead of time because that
7 is -- you know, I'm careful because the press is here and it
8 is a public hearing.

9 So let's try to come up with an alternative that
10 works for everybody that we're being careful with
11 confidential information, but not overstepping our bounds in
12 terms of just excluding the public.

13 MR. CERRITO: Understood. When it comes to
14 this, the rebates and stuff to the PBMs, that's telling them
15 what our pricing is. That is the most competitive
16 information possible.

17 THE COURT: How about if you just gave me a copy
18 of that ahead of time and then when you get to that, you
19 just refer -- you just don't say the specifics, but you tell
20 me to look at page and then I can look at it.

21 MR. CERRITO: I just -- the reason I'm concerned
22 is it's just going to handcuff how I can make my
23 presentation. We have the burden of proof. This is a very
24 important matter. I understand the public has an interest
25 here, my client has an interest here as well and I'm going

1 MR. CALVOSA: I did. I said if you give us
2 yours, we'll give you ours.

3 MS. DURIE: I was going to hand mine out just
4 like they did at the beginning of our presentation.

5 THE COURT: So I think that -- well, if -- let's
6 exchange them. Let's exchange them. So if they're going to
7 give you theirs, you should give them yours.

8 MS. DURIE: Should I hand them up then?

9 THE COURT: Yes. I'll have them both.

10 MR. CERRITO: May it please the Court.
11 Good morning, Your Honor. Nick Cerrito from
12 Quinn Emanuel on behalf of Jazz Pharmaceuticals.

13 Your Honor we're here today because admitted
14 infringer Avadel lost its challenge to the validity of
15 Claim 24 of the '782 patent.

16 On March 4th of this year, the jury found that
17 Avadel failed to prove Claim 24 invalid for lack of written
18 description, lack of enablement and improper inventorship.

19 So at that time Avadel knew it was infringing a
20 valid claim of a Jazz patent. And what did Avadel do?
21 Avadel said it was going to continue to disregard Jazz's
22 constitutional property right. It would continue and has
23 continued to infringe Claim 24.

24 And as Your Honor will hear, Avadel is choosing
25 to willfully infringe, despite telling the world -- and

1 there's several noninfringing alternatives to claim 124.
 2 Jazz's injunction request can be split into two components:
 3 Based on the indications for Jazz's oxybate products and
 4 that request is a limited injunction.

5 The first part of that request is no new Lumryz
 6 prescriptions, they use the dosage form of Claim 24 to
 7 patients who have not already received prescription as of
 8 the effective date of the injunction.

9 The second part would be Avadel is currently
 10 seeking FDA approval for an IH indication idiopathic
 11 hypersomnia; the injunction we seek is in stopping them from
 12 doing that and for marketing IH with a dosage form of
 13 Claim 24.

14 The Court is well familiar with the four factor
 15 test that we're here to deal with today for the permanent
 16 injunction. But regardless, the four-part test is Jazz must
 17 show by a preponderance of the evidence that it has suffered
 18 irreparable injury. The remedies available at loss such as
 19 monetary damages are inadequate to compensate for that
 20 injury. Considering the balance of hardships between the
 21 plaintiff and defendant, a remedy of equity is warranted and
 22 for -- the public interest would not be just served by a
 23 permanent injunction.

24 Even post-*E-bay*, the Federal Circuit has
 25 recognized that this four factor test proceeds under long

1 tradition of equity practice granting injunctive relief upon
 2 finding infringement in the vast majority of patent cases.

3 So let's begin with the first factor, Your
 4 Honor, irreparable harm. Jazz has and would continue to
 5 experience irreparable harm in three ways: Loss of market
 6 share to its direct competitor; two, price erosion; and,
 7 three, repetitional harm and loss of customer goodwill.

8 Further, as I'll explain, there's a causal nexus
 9 between the infringement and the harm because there is at
 10 very least some connection between infringing -- and, again,
 11 I'll say it when we get to it, it's not a close call.
 12 There's at least some connection between infringing features
 13 of Lumryz and the demand for the product.

14 So let's begin with loss market share to a
 15 direct competitor. The evidence will show that Jazz is not
 16 just losing sales. Jazz is losing market share to its
 17 direct competitor who is using our invention.

18 As this court recently found in the *Natera* case,
 19 loss market share to a direct competitor strongly suggests
 20 irreparable harm, and that's based on the Federal Circuit
 21 repeatedly finding irreparable harm under those
 22 circumstances, and including the *Broadcom* case that we cite
 23 here.

24 Now, Avadel may argue that Jazz doesn't practice
 25 Claim 24, you've heard a lot about that. And Your

1 Honor found -- as Your Honor found in *Natera*, there's still
 2 irreparable harm where the parties are direct competitors
 3 and the infringer is taking the patentee's market share, and
 4 that's what we have here.

5 THE COURT: So when Avadel says that Jazz
 6 doesn't practice Claim 24, is that because Xyrem and Xywav
 7 don't use immediate and modified release?

8 MR. CERRITO: That's correct, Your Honor. Here
 9 Jazz is a not a nonpracticing entity, it is a practicing
 10 entity in this case. Jazz has been the market leader in
 11 sleep theory for oxybates. It has two oxybate products that
 12 you heard a lot about at trial, it is Xyrem, which is
 13 100 percent sodium oxybate; and Xywav what is 92 percent
 14 reduced sodium version that the FDA found to be clinically
 15 superior to the 100 percent sodium oxybate product. Xywav
 16 is still in its infancy, it's been on the market for under
 17 four years and is building patient base in the narcolepsy
 18 market, but more importantly in the IH market.

19 In fact Xywav is the first and only approved
 20 treatment for IH. As we'll discuss, IH is a distinct
 21 disorder for narcolepsy; patients experience deep sleep as
 22 opposed to interrupted sleep, but despite sleeping for up to
 23 12 hours, they don't wake up refreshed. And narcolepsy is
 24 obviously opposite, constant wake -- as Your Honor heard
 25 during trial -- they wake up multiple times, if not 40 to 80

1 times a night. And there's several peer-reviewed
 2 publications Jazz has cited that discuss the different
 3 between the two disorders.

4 Avadel has taken and says it will continue
 5 taking Jazz patients and switching them to Lumryz, and
 6 that's both for Xyrem and Xywav. And for Xywav, more
 7 specifically for the narcolepsy and IH. In addition, Avadel
 8 is targeting oxybate naive patients, patients who have never
 9 been on an oxybate product, who hopes they will use Lumryz
 10 over Jazz's products.

11 Here we have Avadel's CEO, Greg Divis, Your
 12 Honor heard him testify at trial. He said that "Avadel's
 13 primary goal is to switch Jazz's patients to Lumryz."

14 Next slide. And that's been the case. Shortly
 15 after Avadel's June launch, as you can see on the top half
 16 of this slide, Avadel reported 74 percent of Lumryz's
 17 prescriptions came from switched patients. And that's
 18 because Avadel's marketing focus -- as you can see on the
 19 bottom part here -- was on the approximately 1600 high
 20 volume oxybate prescribers. Avadel was specifically
 21 targeting them and advocating for them to switch patients
 22 from Jazz's products to Lumryz, and to start new patients on
 23 Lumryz instead of Jazz's products.

24 And Avadel's target for switching patients has
 25 continued. Here we have Avadel's Chief Commercial Officer

1 speaking in a March 2024 BioPharma conference, and he
 2 confirmed that the majority of Lumryz patients are still,
 3 quote, switched patients.
 4 And what's more, more of those patients are
 5 switching from Jazz's low sodium Xywav then from Xyrem.
 6 Avadel's opposition of its lawyer and its
 7 declarant Mohan Rao that Jazz can't prove Lumryz's
 8 prescriptions are coming from switched patients instead of
 9 discontinued Jazz patients.
 10 We have objected to the declaration of Dr. Rao
 11 for a number of reasons, including he was not disclosed in
 12 the pretrial order disclosures. Never had an opportunity to
 13 take his deposition, obviously it's hearsay. Regardless,
 14 it's entirely unsupported by the arguments.
 15 Both Jazz and Avadel track separately, Jazz --
 16 RX coming from switched and discontinued patients. Here in
 17 the same March 2024 presentation where Avadel's COO said
 18 most prescriptions were from switched patients. He also
 19 made clear that Avadel distinguishes switched patients from
 20 new patient who have previously discontinued. And also
 21 oxybate naive patients.
 22 Hold on. It's an internal Jazz document that's
 23 coming up next.
 24 THE COURT: Okay. Let me just take a look at
 25 it.

1 MR. CERRITO: 14, Your Honor.
 2 Maybe I can describe it to Your Honor?
 3 THE COURT: Yes.
 4 MR. CERRITO: So Jazz makes the same
 5 distinctions in its internal documents, switched patients
 6 versus other types of patients. Here -- and what Your Honor
 7 is looking at -- is a tracker. Lumryz's prescription as of
 8 the week ending April 1. And you can see on the far
 9 right-hand side there's sort of a median cliff there, the
 10 reason it's one day, it's not the whole month it's just
 11 April 1st.
 12 If you drop off and you see -- that's the drop
 13 off you see at the end. But what you see here, the blue
 14 line, the one at the top there, that's the -- most Lumryz's
 15 prescriptions are switched from Xyrem, that's what that blue
 16 line shows. The orange line shows Lumryz's prescriptions
 17 that are switches from Xyrem. The gray line at the bottom
 18 switches from Xyrem AG that Jazz gets revenue from through a
 19 royalty. And the yellow are Lumryz prescriptions coming
 20 from patients who previously discontinued Jazz products or
 21 never took Jazz products at all. The discontinuation can be
 22 for any reason.
 23 So Jazz is not -- so Jazz is no doubt losing
 24 revenue from all patient switches; and new patient
 25 opportunities and those that are oxybate naive.

1 Hold on this one as well. It's okay.
 2 Losing oxybate patients is significant to Jazz.
 3 In 2023, Jazz's Xyrem and Xywav made up about 48 percent of
 4 the company's entire revenue. And as we discussed in the
 5 brief because Xywav is still in its infancy, it is growing
 6 in the market, this is a crucial point in its life cycle.
 7 As I mentioned earlier, Xywav has a unique place
 8 in the market. Not only is it the first and only low sodium
 9 oxybate product, it's also the first and only FDA-approved
 10 treatment for IH. Only one.
 11 Now Avadel and its prescriber declarants, which
 12 we again objected to, say that narcolepsy and IH are not
 13 distinct diseases. There's absolutely no support for that.
 14 None.
 15 We've included several peer-reviewed
 16 publications definitively disproving Avadel's unsupported
 17 assertion. And obviously the FDA thinks they are different.
 18 They have different indications than narcolepsy, they
 19 require different clinical trials than narcolepsy; they're
 20 different. And when you look at the peer-reviewed articles,
 21 the peer-reviewed articles make it plain.
 22 17, please. Here it says: Idiopathic
 23 hypersomnia, IH, has been distinguished from narcolepsy on
 24 the basis of the presence of prolonged rather than short
 25 durational sleep periods. And the absence of both cataplexy

1 and episodes of rapid eye movement on the onset of sleep.
 2 Nocturnal sleep is typically disrupted in narcolepsy whereas
 3 idiopathic hypersomnia is prolonged.
 4 And here on the next slide is is Avadel's CEO,
 5 Mr. Divis again, acknowledging huge market opportunity and
 6 how the only FDA-approved product Xywav is only in its
 7 infancy; less than 10 percent market penetration. But
 8 there's a robust patient population and the market is
 9 growing. And it's consistent with the literature we just
 10 looked at, Avadel's own CEO admits that IH is different than
 11 narcolepsy.
 12 And Jazz saw growth of Xywav and IH, and
 13 specifically IH in 2023. It increased to 59 percent from
 14 2022. That IH market continues to grow.
 15 Like the *Illumina* case we cited, the Xywav
 16 market and, in particular, IH is a crucial inflection point
 17 and Jazz is suffering and will continue to suffer
 18 irreparable harm if Avadel were allowed to capture the IH
 19 market by using Jazz's Claim 24 technology.
 20 We've also seen Avadel -- and you'll hear them
 21 argue -- that Lumryz was supposedly to provide some
 22 advantage over Xywav for IH, because Lumryz is a
 23 once-nightly oxybate. Guess what? Xywav is already
 24 approved for once-nightly.
 25 There's no evidence that there's some kind of

1 superiority to Lumryz in this particular market; no evidence
 2 at all. It's pure speculation. They don't have an
 3 approved product, they haven't filed for an approved
 4 product.
 5 The FDA determined that Jazz's Xywav is safe and
 6 effective for a once-nightly treatment of IH, specifically
 7 including one nightly dosing instructions for IH in that
 8 Xywav label. Moreover, Jazz's Xywav has 92 percent less
 9 sodium than Lumryz, so it's even safer than Lumryz.
 10 And the data, of course, is consistent with the
 11 FDA's determination and the approval of Xywav once-nightly
 12 for IH. This is a peer-reviewed publication that we're
 13 seeing from the clinical study that gained Xywav market
 14 approval for IH. And on this slide we'll see the
 15 conclusions the author made consistent with that which the
 16 FDA reached, and that conclusion is the efficacy results
 17 were similar across two different dosing regem subgroups:
 18 Once-nightly and twice-nightly.
 19 So unlike Dr. Stern's unsupported declaration
 20 where Avadel just says, shockingly, without any citation,
 21 without any support, once-nightly doesn't work, Xywav. You
 22 would think they would cite something for that. And then
 23 nobody uses it for that.
 24 The FDA and the peer-reviewed publications say
 25 otherwise. We may see Avadel put up some data from the FDA

1 (Sealed.)

1 review, and if they I'll show Avadel submitted a truncated
 2 version -- this is one of the late submissions they made and
 3 didn't give Your Honor all the information. And it omitted
 4 portions that show the FDA, unsurprisingly, reached the same
 5 conclusion as the authors of the peer-reviewed. Again, the
 6 efficacy results were similar across two different dosing
 7 regem subgroups, once- and twice-nightly.
 8 So Jazz is experiencing irreparable harm through
 9 loss of market share to its direct competitor, Avadel.
 10 Willfully and illegally using Jazz's technology of Claim 24.
 11 That irreparable harm will continue through expiration of
 12 the '782 patent in 2036, so even if Avadel gets its approval
 13 or doesn't get its approval -- or gets its approval in 2027
 14 like it alleges it will, that still gives us nine years of
 15 willful infringement of Jazz's patents.
 16 Let's move on to price erosion. And this is
 17 where we might have to clear the courtroom, Your Honor.
 18 THE COURT: All right. This is going to get
 19 into a sensitive area, so I'm going to need to clear the
 20 courtroom of -- do you need Avadel's client representatives;
 21 is that what you're asking for?
 22 MR. CERRITO: Anyone who is not under the
 23 protective order, Your Honor.
 24 THE COURT: Anyone who is not under the
 25 protective order needs to leave the room, please.

There are two ways Jazz is experiencing repetitional harm and loss of goodwill. The first is a loss of status as exclusive market leader. The Federal Circuit recognized in *Celsis* that losing the ability to market oneself is an exclusion of market leader is irreparable harm. And further recognized this harm is particularly crucial during the growth stage of the product, such as the

25 Here we have *EZ Guard* case showing that an

1 infringer using patented technology to market itself as
 2 having a superior product is repetitional harm. Avadel is
 3 using Jazz's Claim 24 to do just that. And while Jazz
 4 disagrees and is challenging the Lumryz superiority finding,
 5 it is not as broad as Avadel attempts to make it seem.
 6 Instead, it is limited to narcolepsy patients. It does not
 7 apply to IH patients at all. And it is limited to
 8 narcolepsy patients who are not salt-sensitive.

9 For Xywav, the FDA itself concluded the
 10 difference in sodium content is clinically meaningful. That
 11 Xywav will be the drug of choice in salt-sensitive patients.
 12 Those salt-sensitive patients are a significant portion of
 13 the narcolepsy population and reduction of sodium would be
 14 clinically meaningful in all narcolepsy patients, not just
 15 those that are salt-sensitive.

16 Contrary to the FDA, Avadel's messaging focuses
 17 on saying that sodium is not a concern. I don't know about
 18 Your Honor, but when I go to the doctor I hear all about
 19 salt being a concern.

20 THE COURT: Well, didn't the FDA also make some
 21 statements about it had already -- do you dispute that the
 22 FDA said -- the FDA has already factored in the safety risk
 23 associated with the differences in the content of sodium
 24 between Lumryz and Xywav and concluded that Lumryz makes a
 25 major contribution to patient care.

1 MR. CERRITO: But not in safety, Your Honor, and
 2 not in efficacy. Simply convenience, which I'll get to in a
 3 minute. It's not safer. It has the 100 percent sodium
 4 oxybate in it. The 92 reduced sodium oxybate product is
 5 Xywav. They never said it's safer. In fact, they said if
 6 you're salt-sensitive, you should Xywav.

7 THE COURT: Did they say that benefit also by
 8 once-nightly dosing would outweigh the risk of increased
 9 sodium intake because disruptive sleep is antithetical to
 10 the goals of oxybate treatment.

11 MR. CERRITO: But not in salt-sensitive
 12 patients -- and, quite frankly, this is part of the argument
 13 that we're hearing in DC is about, right. They say on one
 14 hand it's more important, but salt-sensitive you should use
 15 Xywav, which is it.

16 I'll get to the fact -- Your Honor asked a great
 17 question. We'll get to the -- what we have from the FDA was
 18 a statement prelaunch. I'm going to show you what's
 19 actually happening in the marketplace, how the product isn't
 20 working the way everybody thought it was going to. I have
 21 actual data in a second.

22 THE COURT: Okay.

23 MR. CERRITO: So contrary to the FDA, Avadel was
 24 focused again saying sodium is not a concern. And that's
 25 what Avadel says in a competitive messaging strategy and

1 internal documents, and that's what Avadel is telling
 2 consumers. In fact, Avadel even funded a paper that says
 3 that "sodium oxybate treatment does not confer additional
 4 cardiovascular risk of narcolepsy as opposed to Xywav."
 5 Again, it's not what the FDA concluded.

6 So Mr. Honerkamp explained, contrary marketing
 7 by Avadel harms Jazz's repetition as a trusted source of
 8 sleep disorder-related information.

9 Let's move now to the casual nexus. As we said
 10 in our briefs, and I said earlier today, it's not a close
 11 call on this one. But let's go through it.

12 In *Apple v. Samsung*, the Federal Circuit held
 13 that there need only be some connection between infringing
 14 features and the demand for the infringing product. The
 15 infringing features do not need to be predominant or
 16 exclusive reason why consumers are buying the product. Here
 17 there could be no doubt no matter which standard is applied
 18 Jazz satisfies it.

19 As Avadel's counsel admitted during opening
 20 statements in this case, there is no Lumryz without the
 21 invention of Claim 24. In fact, Avadel's counsel tried to
 22 say that Claim 24 was Avadel's invention. The jury, of
 23 course, disagreed and rejected that argument. But there can
 24 be no doubt that Claim 24 covers Lumryz as a whole. This
 25 was confirmed by Jazz's technical expert, Dr. Little, at

1 trial. Claim 24 matches up with Lumryz as a whole. Avadel
 2 has not put forth any evidence to the contrary.

3 Well, in the damages space, the Federal
 4 Circuit's decision in *AstraZeneca* is instructive I think.
 5 There the Court held a formulation claim that covered a
 6 product as a whole and allowed the product to be marketed
 7 could not be broken up into novel elements versus elements
 8 in the prior art. It recognized pharmaceutical formulations
 9 is not the same as a multi-component product, like a
 10 cellphone where one feature may be the patented product and
 11 the rest of it isn't. Similar here there's not a case where
 12 Claim 24 covers a single component of a multi-component
 13 product. Claim 24 covers Lumryz as a whole.

14 The Federal Circuit has also applied this
 15 reasoning in injunction context for other pharmaceutical
 16 products at issue. I cite the Court to *Mylan v. Aurobindo*
 17 857 F.3d 858, pin site 72-73 -- 872-73 (Fed. Cir. 2017.)

18 Moreover, despite Avadel's attempt to now
 19 belittle the invention of Claim 24 and reduce it only to
 20 sachet packaging, Claim 24 adds much more to the prior art
 21 than that. Unrebutted evidence shows that Claim 24 the
 22 addition of the viscosity-enhancing agent in the acid,
 23 separate from the oxybate particles in the sachet is what
 24 allows in combination of IR and MR oxybate particles to be
 25 taken by the patient and remain stable so that there's no

1 oxybate overdose. We have seen nothing to dispute this
 2 major advanced discovery by Mr. Allphin.
 3 And by the way as a side note, if this whole
 4 invention is about a sachet, why don't they just change
 5 the -- change the dosage. They can change the form and we
 6 wouldn't be here. I think there's a little bit more than
 7 just the sachet.

8 To sum up, Jazz submits that it has shown
 9 irreparable harm by more than a preponderance of the
 10 evidence. Jazz has lost market share to direct competitors,
 11 Avadel. Avadel is using Jazz's technology to cause price
 12 erosion and will continue to do so in the future. Jazz is
 13 suffering reputational harm and loss of goodwill. And
 14 there's no doubt that at the very least some connection and
 15 therefore a casual nexus between Claim 24 and the sales of
 16 Lumryz.

17 Next I want to move on to why monetary damages
 18 are inadequate to compensate Jazz. And I'll note that
 19 Avadel's declarant, Dr. Rao, offers no opinion, none
 20 whatsoever, that monetary damages are adequate to compensate
 21 Jazz if irreparable harm is found. He offers no opinion on
 22 that, Your Honor.

23 As Your Honor recognized in *Natera*, this factor
 24 is nearly indistinguishable from irreparable harm. The
 25 Federal Circuit has found in *i4i*, for example, the loss of

1 market share, consumer goodwill, etc... frequently defy
 2 attempts at valuation, particularly where the infringing
 3 acts are changing the market, as is happening here clearly.
 4 The Federal Circuit has held monetary damage is
 5 inadequate where the patentee is forced to compete against
 6 their rival, gaining market share with the patentee's
 7 technology, as we have here, and that's the *E.I. DuPont*
 8 case, where the reputational harm -- where there is
 9 reputational harm, like we have here, citing to *Douglas*
 10 *Dynamics*.

11 And contrary to Avadel's argument, the Federal
 12 Circuit explained in *Mytee* that you do not have to establish
 13 that you're entitled to lost profits to show that
 14 irreparable harm and the adequacy of monetary damages.

15 Let's move on to the balance of the hardships.
 16 Under the Federal Circuit law the balance favors Jazz. Jazz
 17 is losing market share and being forced to compete with its
 18 own technology. As the Federal Circuit confirmed in *Apple*
 19 *v. Samsung*, this place is a substantial hardship on the
 20 patentee. Moreover, like in the *Sanofi* Federal Circuit
 21 case, any alleged harm to Avadel was caused by its own
 22 decision to launch at risk. It could have waited. It
 23 didn't have to launch, it could have waited. Could have
 24 seen the outcome of this trial before it launched its
 25 product, it chose not to; that was a risk it took, decision

1 it made.

2 As shown on page 12 of our opening brief, Avadel
 3 specifically told this court that it intended to launch at
 4 risk and would not wait for a jury verdict. Again, that's
 5 their choice. As we discussed shortly, Avadel does not
 6 dispute that it has told the world it has a once-nightly
 7 oxybate dosage forms that do not infringe Claim 24 of the
 8 '789 patent. For whatever reason Avadel is choosing not to
 9 market those.

10 So any harm from Avadel needing to stop
 11 infringing Claim 24 is entirely preventable, it was
 12 preventable in the first place and continues to be
 13 preventable.

14 Here we have several courts, including the
 15 Federal Circuit, noting the importance of potential
 16 noninfringing alternatives, which Avadel does not deny it
 17 has in the balance of hardship analysis.

18 Your Honor made the same observation in *Natera*,
 19 citing *Transamerica v. Lincoln Life*, and it reached the same
 20 conclusion. The balance further tips in the patentee's
 21 favor when noninfringing alternatives exist.

22 So we heard at trial Dr. Guillard and Ms. Megret
 23 purport to have developed the unit dosage forms in the '062
 24 patent, that was the Avadel opener. Here we see the first
 25 principle embodiment of Avadel '062 patent does not have

1 either a viscosity-enhancing agent or as an acid as a
 2 component. It only shows up in the second principle
 3 embodiment.

4 Despite its multiple trial witnesses, numerous
 5 declarants for injunction briefing, Avadel never provides an
 6 explanation of why it will not now use a dosage form that
 7 would not infringe Claim 24; despite telling the world it
 8 has such dosage forms. They want to just continually
 9 willful infringe.

10 Same is true with Claim 24 sachet element.
 11 Again, why didn't they just change it. That's all this is,
 12 just change. Avadel's patent says it. It says "The present
 13 invention can be provided in any dosage form that is
 14 suitable for oral administration." And that lists a long
 15 list of options, the sachet being just one.

16 Moreover, Avadel's decision to be a one-product
 17 company is exactly that, Avadel's decision. They stand
 18 before this court and say it's an existential threat to
 19 their existence. It's based on their choices. They didn't
 20 have to be a one-product company. They didn't have to
 21 launch at risk. They didn't have to come in and tell us,
 22 this court, that they were the inventors of it. The jury
 23 told them they were wrong. All these decisions were wrong.
 24 That's their fault. Jazz shouldn't be punished for their
 25 mistakes.

1 Avadel decided that it wanted to focus
2 singularly on Lumryz and divest all other products, that's
3 their fault, that was their decision. Avadel has not cited
4 and we have not been able to find a single case where an
5 injunction was denied and the balance of hardship tips in
6 the favor of the now willful infringer where such facts
7 exist. There's no case out there. Again, all these
8 decisions were made by them. Turns out they weren't great
9 decisions, but that's not Jazz's fault.

10 Instead, the Federal Circuit has repeatedly
11 held, including in the *Windsurfing* and *Robert Bosch* case
12 that "a party cannot avoid an injunction simply because it's
13 smaller than the patentee or because it chose to build its
14 business on an infringing product." That's exactly what
15 happened here. Avadel knew about Claim 24 before it
16 launched, didn't come out after, they weren't surprised,
17 they knew it. Told the world they had other versions of
18 Lumryz that do not infringe Claim 24, presumably they are
19 not lying in the patent, presumably they are telling the
20 truth. But Avadel chose and continues to choose to infringe
21 Jazz's property right and uses Jazz technologies to Jazz's
22 irreparable harm.

23 The last factor, Your Honor, in the permanent
24 injunction analysis is whether the specific limited
25 injunction Jazz requests would disserve the public interest.

1 Talked a little bit about this when it came to choice. And
2 I'll harp on it again.

3 THE COURT: Let me ask you some questions with
4 this one.

5 MR. CERRITO: Yes, Your Honor.

6 THE COURT: Do you see a difference with respect
7 to narcolepsy and IH, in that -- am I correct that a use for
8 Lumryz with respect to IH at the present time is off-label
9 use?

10 MR. CERRITO: That's correct, Your Honor.

11 THE COURT: With respect to narcolepsy, it's
12 a/an consistent with label use.

13 MR. CERRITO: Yes, Your Honor.

14 THE COURT: And it's been in the market --

15 MR. CERRITO: About a year now.

16 THE COURT: About a year now. And the FDA
17 has -- you know, the distinguishing factor is the
18 once-nightly versus the two doses nightly. I get the
19 distinction, Xywav has less sodium. But from a public
20 interest standpoint, do you see any difference between
21 narcolepsy and IH?

22 MR. CERRITO: Well, certainly. I mean, first of
23 all, they are two different diseases, obviously.

24 THE COURT: Right.

25 MR. CERRITO: Secondly --

1 THE COURT: But with respect to protecting the
2 interest of the public --

3 MR. CERRITO: They don't have a -- one, they
4 don't have a product obviously yet. But they don't have
5 what would be a superior once-nightly because Jazz has a
6 once-nightly. We can supply the whole market with the
7 once-nightly product, there's no difference in convenience.
8 Same.

9 THE COURT: With respect to IH?

10 MR. CERRITO: Correct, Your Honor.

11 THE COURT: So when it comes to the public
12 interest, Avadel doesn't have an advantage because Xywav has
13 been approved for once-nightly?

14 MR. CERRITO: Yes.

15 THE COURT: But with respect to narcolepsy,
16 there's a difference, right?

17 MR. CERRITO: I'm not going to trick you into
18 saying we do have an advantage, but I still disagree. Yeah,
19 there's a difference, Your Honor, clearly. I mean, there is
20 a difference.

21 I understand that the once-nightly pre-approval
22 superiority finding is there. I get it.

23 What we're seeing in the marketplace is it's not
24 reality. And I'll -- maybe I should jump to that right now.

25 THE COURT: Okay. You can continue how you want

1 to continue --

2 MR. CERRITO: I know but I want to get it to. I
3 keep telling you I'm going to get to it, but I haven't
4 gotten to it. I'm going to get to it.

5 Yeah, there's a difference, but that doesn't
6 mean patentee's rights should be thrown in the garbage.
7 Again, it's not a safer product. It's not a more effective
8 product. In fact, in some instance, less effective,
9 especially for salt-sensitive patients. The interest is
10 slightly different in the IH market, obviously that's true,
11 but I don't think it's a compelling difference.

12 THE COURT: Okay.

13 MR. CERRITO: So let me continue, Your Honor.

14 Public interest factor requires balancing the
15 public's interest and protecting the patentee's
16 constitutionally granted rights in the public interest and
17 the adverse effects of the injunction.

18 And we'll talk -- let me -- trying to get ahead
19 of myself. The Federal Circuit explained in *Apple v.*
20 *Samsung* that the public interest strongly favors an
21 injunction because public interest strongly favors
22 investment property rights and reoccurring innovation, and
23 nowhere is more true in the pharmaceutical industry.
24 Nowhere is that more true.

25 THE COURT: Right. Right.

1 MR. CERRITO: Whether we have the new cellphone,
2 who cares. If we have life-saving products that matters.

3 THE COURT: But you recognize the decisions by
4 Judge Dyke and those other decisions, including one by Judge
5 Norieka out of this district, that in the pharmaceutical
6 context public interest is a significant factor, and
7 particularly when one of the drugs has some distinguishing
8 feature --

9 MR. CERRITO: And that's a great point, Your
10 Honor. And, look, I don't envy you, this case is all over
11 the place, right. You can pick and choose all you want.
12 We're going to focus on a couple that I think are relevant.

13 When it comes to distinguishing feature, those
14 cases that go either way are distinguished based on efficacy
15 or safety. There is no decision going against us on
16 convenience. In fact, the only other case on convenience
17 that exists is the *Amgen* case, and that rules in our favor.
18 They say patient convenience, it doesn't matter. That's
19 what they said in *Amgen*, and I'm happy to talk through that
20 right now, Your Honor.

21 THE COURT: Wasn't --

22 MR. CERRITO: *Amgen v. Hoffmann-La Roche*, Your
23 Honor.

24 THE COURT: Wasn't there an issue that has to be
25 --

1 THE COURT: If a provider, a physician,
2 whatever, believes that his patient, his or her patient is
3 better off or more likely to comply with a once-nightly
4 formulation as opposed to a twice-nightly formulation -- it
5 may not be true. It may not be safer, more -- may not have
6 greater efficacy, but for whatever reason the provider
7 thinks that, then that --

8 MR. CERRITO: When you say "thinks that" -- and
9 I'm going to cut to the chase. I'm going to stop teasing
10 and get to the point. What you're seeing is, in the market
11 place -- can we go to slide 66, please. This is all --
12 remember this is all pre-approval discussion. We think it's
13 easier, once-nightly sounds better than twice. What you're
14 seeing -- look at the bottom there, Your Honor, 1700
15 prescriptions, there are 1400 patients on drug now, so 300
16 dropped off. I don't know what happened to them, could be
17 any factor, but 300 no longer. 630 adverse events. And the
18 second bullet point that says "300-plus reports of insomnia"
19 -- you know what insomnia is, you get no sleep. Drug
20 ineffectiveness. It doesn't work.

21 And when these people wake up in the middle of
22 the night with once dosage, they can't take another dose,
23 because it would put them over the top, the amount would be
24 dangerous, they could die. So when they wake up in the
25 middle of the night, they're done; they are up for the

1 MR. CERRITO: It was twice a week -- once every
2 two-week dosing versus once-a-month dosing, so more
3 convenient, but technically the less infringing product.
4 And the Court said that wasn't good enough.

5 THE COURT: The *Baxalta*, the *Baxalta* case that
6 had the difference in --

7 MR. CERRITO: I think there was a couple of
8 things going in *Baxalta* that distinguish it. Again, a very
9 short lifetime left on the patent. Some of the other
10 factors didn't weigh in the same way they do here.

11 But, again, if you look at *Amgen v. Hoffmann-La*
12 *Roche* twice a -- once every two weeks versus once monthly,
13 the more convenient dosage wasn't married to the injunction,
14 it simply wasn't. Where it comes down to public interest is
15 where that product is slightly more effective or safer.
16 That makes sense. More convenient doesn't -- we don't --
17 there's not a single case that says more convenient is a
18 factor that you need to weigh in denying an injunction.
19 Doesn't exist.

20 There is one case more convenient that rules in
21 our favor. I know they go all over the place, Your Honor.

22 THE COURT: I understand. I understand.

23 From a public interest perspective, if a
24 provider --

25 MR. CERRITO: I'm sorry, Your Honor?

1 night. So this idea that once-nightly was so great
2 pre-launch, pre-actual evidence in the marketplace, didn't
3 turn out to be so true.

4 The doctor's choice -- everybody wants more
5 choices. Great. If that's the case -- as the case law,
6 Your Honor, is well aware of, I'm not telling you something
7 you don't know, we'd never have an injunction in this space
8 then. Choice is always better, right? But that doesn't
9 mean you get to infringe people's property rights to it and
10 stifle investment in future development. That's what
11 happens when you to do that.

12 Choice here is not based on safety, it's not
13 based on efficacy. It's based on oh, I want to do
14 once-nightly until it doesn't work for you and patients drop
15 off, and that's what we're seeing in the actual marketplace.

16 When you talk about doctor's choice, they put in
17 three declarations from the doctors. Interesting they are
18 not high prescribers, they don't say how many people they
19 treat. But what's more interesting is they say they don't
20 walk away from Xyrem or Xywav. They aren't saying that's a
21 problem, they are not saying those drugs don't work. Maybe
22 they get to one of those patients that's the 300 and it
23 didn't work for them and they go back to Xyrem or Xywav.

24 So choice in and of itself, again looking at the
25 *Amgen* case, is not a basis. There's never been that I'm

1 aware of an no case cited to Your Honor where choice alone
2 is the driving factor in denying an injunction. It's just
3 not.

4 And when you look at the patient -- and with all
5 due respects to patients, I know they are suffering and
6 these are people that are very important to our client as
7 well, both clients care about them very much, look at what
8 they said. What they say is: I took Xyrem, it was
9 life-changing, changed their life. Now they say the same
10 thing about Lumryz. They'll switch back later and say it
11 again about Xyrem, who knows. There is no distinction
12 between safety and efficacy of these two drugs. That's what
13 matters. They are the same. And in certain instances
14 Lumryz -- with regard to Xywav, it's safer, less sodium,
15 less sodium. That's the reality.

16 So the case law -- in *Baxalta* there was a
17 substantial merits question there as well why it was
18 rejected, I think. As Your Honor well knows a preliminary
19 injunction most cases if you can't meet the likelihood of
20 success on the merit, you're not getting to the other steps.
21 I know the Court's analyze them, but you can't win that one.
22 You're not winning. So I think those are distinguishable.

23 Again, no case law that I'm aware of that was
24 cited by anybody where choice was the reason to deny the
25 injunction.

1 So returning, Your Honor, briefly, the Federal
2 Circuit explained in *Sanofi* that there's a significant
3 public interest and encouraging investment in drug
4 development. That interest tips in the favor of the
5 patentee here.

6 Moreover, Avadel has not cited one case and Jazz
7 hasn't found any case where the Court has denied an
8 injunction where a possible noninfringing alternative
9 exists. They have one, they've told the world they have
10 one, they don't want to use it. They want to just keep
11 infringing ours.

12 Jazz has provided the court with numerous
13 examples of the opposite. And there are two on the slide
14 here, *Transamerica Life* and *SynQor*. Any alleged harm to the
15 public for the injunction, which Jazz disputes exists, can't
16 be mitigated by Avadel using a noninfringing alternative to
17 Claim 24 formulation.

18 Moreover, most of Avadel's cases cited in the
19 context again of preliminary injunction where there was a
20 substantial question of whether or not the patent was valid
21 and/or infringed. In the permanent injunction cases, there
22 are also -- aside from the public interest weighing against
23 the injunction, but each of Avadel's cited cases a public
24 interest weighed against an injunction because a greater
25 safety or efficacy of pharmaceutical -- mostly of

1 life-saving situations. This is clearly not that case.

2 Standing again on the case that's on our fours,
3 we believe is *Amgen*. I won't bore Your Honor again and go
4 through it, but that one is -- it's not on all fours, it was
5 once a month versus once every two weeks, convenience
6 dosing. But, again, there was no clear -- the Court found
7 that there were no clear safety or efficacy benefits. Same
8 here. Same here.

9 They also found, like we talked about in our
10 reply brief --

11 (Discussion held off the record.)

12 The *Amgen* case -- *Amgen v. Hoffmann-La Roche* 581
13 F.Supp.2d 160 (D.Mass.2008).

14 They found -- we talk about this in our reply
15 brief that because of the short time the infringing product
16 was being used, there was insufficient data to say more
17 convenient dosing would be more effective in the long run.
18 And that's what I think I just showed you, Your Honor. We
19 have a very small dataset for one year of dosing. We've got
20 the number of patients up there with 300 showing it's not
21 effective. That's what's happening in the actual consumer
22 market.

23 Again, Your Honor pointed out the superiority
24 finding. I'm sure Avadel will come up here and talk quite a
25 bit about that. Remember that's being reviewed as we speak

1 by the DC court right now, Judge Mehta. But if you look at
2 this slide 66, please. Lumryz in clinical superiority
3 finding was limited to nonsalt-sensitive narcolepsy
4 patients. Lumryz FDA clinical superiority finding do not
5 address IH patients at all. Lumryz is not life-saving.
6 Lumryz is not more effective than Jazz's products. It's not
7 safer than Jazz's products.

8 Again, all the alleged side effects, we see
9 there, 630 adverse events on 1700 scripts. All stuff they
10 complain about with Xyrem and Xywav they're finding out to
11 be exactly the same. And critically important the 300
12 reports of insomnia/drug ineffectiveness. And those
13 patients, as I said, wake up in the middle of the night,
14 they can't take another dose. They have to just stay up.

15 Xywav is safer to Lumryz due to its
16 significantly reduced sodium burden. Xywav is already
17 FDA-approved for once-nightly treatment for IH and is
18 clinically shown to be effective for once-nightly treatment
19 of IH.

20 Avadel's prescriber and patient declarants do
21 not change facts or the law here. The Federal Circuit held
22 in *Mallinckrodt* that such testimony cannot be interpreted,
23 it represents the majority of the doctors. Talked about
24 this briefly. They describe three prescriber declarants,
25 there are approximately 1600 high prescribers of oxybate.

1 Neither declarants nor Avadel provide any evidence on how
2 the oxybate patents prescriber declarants actually have; how
3 many dosing they are doing there. They don't say they're an
4 oxybate high prescriber.

5 At most the declarants allege that these couple
6 of prescriptions in patients want a choice of drugs, even
7 though each patient was getting symptom relief with Jazz's
8 products. Most notably, the prescriber declarants do not
9 say they're going to stop using Jazz's products. They don't
10 say that. Avadel is going to do everything it can to switch
11 them, but they didn't say that.

12 And remember the slide we just looked at all the
13 alleged problems with Avadel's complaints about Jazz's
14 product exist with Lumryz. Convenience doesn't really seem
15 to be a factor.

16 As the Federal Circuit has held eliminating
17 choice of drugs is not by itself sufficient to divest the
18 public interest. Under such approach, courts would never
19 injoin a drug because doing so would always reduce choice.

20 The Federal Circuit further explains in *WBIP v.*
21 *Kohler* that even for life-savers reduction in choice does
22 not warrant denying an injunction.

23 For all these reasons, Your Honor, Jazz submits
24 that it has met its burden for permanent injunction.

25 Before I sit down, Your Honor, just briefly,

1 stabilizes the product so the product is able to be taken by
2 patients, and there was basis for the approval. It also
3 gives it availability to be administrable. You heard about
4 that from Dr. Little at trial because of the separateness
5 and the way he put it in the sachet patients are able to
6 take it. So 100 percent it covers the entire product, not
7 just an element of the product.

8 THE COURT: These patents that Jazz licensed to
9 the generics.

10 MR. CERRITO: Yes.

11 THE COURT: Let me understand. So if Jazz
12 hadn't come up with the patent for the use of a unit dosage
13 form of sodium oxybate or did it just come up with specific
14 formulations of the unit dosage form recited in Claims 14
15 and 24?

16 MR. CERRITO: I'm confused only because you said
17 the license. Those have --

18 THE COURT: Did Jazz originally come up with
19 the -- does one of Jazz's prior patents --

20 MR. CERRITO: The patents that were licensed
21 have nothing to do with this technology.

22 THE COURT: Okay.

23 MR. CERRITO: It's different patents that cover
24 other aspects.

25 THE COURT: So Jazz didn't invent the use of

1 final point is Avadel's unpled, newly founded unclean hands
2 defense. As this district has previously found in *Bench*
3 *Walk Lighting*, unpled, unclean hands defenses are waved.
4 Unclean hands defenses is subject to Fed RCP 9(b), must be
5 pled with particularity. When unclean hands defense isn't
6 pled with any facts at all, such as the case here, it is
7 undoubtedly waved. Moreover, Avadel's new defense is
8 baseless. Avadel hasn't proven nor could show that Jazz
9 acted with unclean hands.

10 Before we go on to the ongoing royalty, I'm
11 going to sit down.

12 THE COURT: All right. Let me ask you some
13 questions.

14 MR. CERRITO: Yes, Your Honor.

15 THE COURT: All right. Just so that we're clear
16 for the record. Explain to me what the improvement of
17 Claim 14 and 24 of the '782 patent was over the prior art.

18 MR. CERRITO: It was combining the
19 viscosity-enhancing agent separate from the immediate
20 release particles in a combination in a sachet. It was a
21 combination of all of those elements.

22 THE COURT: Okay. And does that improvement
23 factor into why patients use Lumryz?

24 MR. CERRITO: Multiple ways. One the product
25 wouldn't exist, obviously, without all that. Two, it

1 sodium oxybate in any unit dosage?

2 MR. CERRITO: We do have -- the original patents
3 that we had now expired, we did come up with a unit -- there
4 was a -- the original patents on using the formulation --
5 there was an original formulation back 100 years -- not
6 100 years ago, a while ago that now expired. I apologize,
7 I'm not sure what you're asking.

8 THE COURT: All right.

9 MR. CERRITO: That was a different technology,
10 didn't involve it. It was just an amount of how you had to
11 dilute it for storage and stuff like that.

12 THE COURT: Okay. All right.

13 MR. CERRITO: That was the immediate release
14 product Xyrem.

15 THE COURT: Xyrem.

16 MR. CERRITO: That was the patents that were
17 licensed in the other case, it had nothing to do with this.

18 THE COURT: All right. And the patents that you
19 licensed to the generics, do they cover Xyrem and Xywav?

20 MR. CERRITO: They -- well, they have nothing to
21 do with Xywav.

22 THE COURT: Okay.

23 MR. CERRITO: The cases -- the cases on Xyrem --
24 and there were certain -- the patents covered drug-drug
25 interactions with regard to Xyrem. It has nothing to do

1 with -- there's ongoing litigation with Xywav. The license
2 on patents has nothing to do with it. The original
3 litigations with Xyrem go back to 2010, and we did license
4 what we called "drug-drug interaction patents." When you
5 take this product because of the sedative effectiveness with
6 other products it can cause a compounding effect, obviously
7 can be very dangerous.

8 THE COURT: The generics are they the generics
9 of Xyrem only or Xyrem or Xywav?

10 MR. CERRITO: Only Xyrem.

11 Xywav is ongoing litigation now.

12 THE COURT: Okay. Before the '782 patent, was
13 it known in the prior art to combine a viscosity agent and
14 assay and sachet to stabilize a drug?

15 MR. CERRITO: The short answer is no. The
16 reason I pause is any drug -- I apologize I'm trying to be
17 100 accurate. I don't think it is any drug. Certainly with
18 regard to this drug no. In fact, the defendants have
19 dropped it in anticipation of obviousness arguments to that
20 very fact because it wasn't on the prior art.

21 THE COURT: Okay.

22 All right. That answers -- is there anything
23 unique or distinguishable about using a sachet as the unit
24 dose?

25 MR. CERRITO: For any product -- I mean, the

1 Xyrem. That's where we showed you that chart that we didn't
2 publish, the vast majority of the prescriptions are coming
3 from.

4 All right. That's all the questions I have for
5 you.

6 MR. CERRITO: Thank you, Your Honor.

7 MS. DURIE: Good morning, Your Honor. Daralyn
8 Durie for Avadel.

9 As the Court knows, there is a four factor test
10 that governs the issuance of an injunction, and Jazz bears
11 the burden with respect to each of those four factors. Jazz
12 must show that each of those four factors are satisfied in
13 order for an injunction the issue. Each of them is
14 critical, but the Courts are clear that the public interest
15 in particular is critical. And if a plaintiff fails to show
16 that the public interest would not be deserved, it being
17 Jazz's burden to make that showing, than the District Court
18 may not make that injunction.

19 Because the public interest is so critical that
20 is where I would like to begin. Now, first courts have
21 routinely refused to permanently enjoin activities that
22 would injure the public health because the public health is
23 paramount in this inquiry.

24 I want to note this is an important distinction
25 from the *Natera* decision, because in that case the Court

1 existence of the sachet is they existed.

2 THE COURT: Right. They existed before this
3 patent.

4 MR. CERRITO: Correct.

5 THE COURT: At least with respect to other
6 drugs.

7 MR. CERRITO: Correct.

8 THE COURT: But it didn't exist with respect to
9 GHB.

10 MR. CERRITO: That's correct.

11 THE COURT: And so that's part of the invention
12 of Claim 24, is what you're saying?

13 MR. CERRITO: Yes, Your Honor. Along with the
14 viscosity-enhancing agent as separate from the core. The
15 rest of it as well.

16 THE COURT: Okay. So with respect to
17 irreparable harm, some of the lost sales that Jazz is
18 experiencing is coming from the generics, right?

19 MR. CERRITO: Some of the lost sales of Xyrem
20 are coming from generic sales.

21 THE COURT: Yes.

22 MR. CERRITO: It's an authorized generic, it's
23 our product, we get a financial benefit there. But they do
24 not touch Xywav; it has nothing to do with Xywav. And
25 that's why Avadel is focused on Xywav, it hasn't focused on

1 concluded that *Natera's* competitive product appears to be
2 equally accurate, covers all the same diseases, and that
3 *Natera* had sufficient capacity to meet the market's needs.
4 That is not true here.

5 Lumryz has expanded the patient population who
6 can benefit from oxybate. And it has been determined to be
7 clinically superior, clinically superior, medically
8 superior, because of the benefits of once-nightly dosing.
9 And we'll talk about that evidence.

10 I want to talk about that evidence both with
11 respect to narcolepsy and to address the Court's questions
12 with respect to idiopathic hypersomnia, but I want to start
13 by talking about narcolepsy.

14 The premise here is that all narcolepsy patients
15 should have access to Lumryz if it is the treatment that is
16 best for them. Now, court's have refused to grant an
17 injunction when doing so would eliminate an important
18 alternative for patients.

19 Now I want to be clear, counsel is correct that
20 it is not sufficient simply to invoke the phrase "patient
21 choice." Because in the context of a generic drug, for
22 example, where the two products at issue are identical,
23 there is no interest in patient choice because the identical
24 therapy can be received in either -- with either of the two
25 drugs. But here we're talking about two highly

1 differentiated products, and when products are
2 differentiated and provide different benefits to patients,
3 that is when patient choice between those differentiated
4 alternatives becomes paramount.

5 Now, in *Baxalta* the Court noted there and relied
6 on the fact that the FDA had recognized the importance of
7 making the treatment available. In that case, by granting a
8 break-through therapy designation, and the Court found that
9 the product at issue conferred substantial medical benefits
10 over the existing theories. And I would suggest the record
11 here amply supports that same conclusion.

12 As was just being discussed, FDA made a
13 determination that Lumryz is clinically superior to Xywav.
14 In making that determine, the FDA found that waking up to
15 take a second dose of Xyrem and Xywav is antithetical to the
16 goal of improving sleep. It found that even with a single
17 nocturnal arousal, there can be impairment of alertness and
18 decline in cognitive performance the following day. That a
19 person with disrupted sleep cannot simply return to sleep
20 and resume their normal sleep cycle. And that Lumryz,
21 unlike Xywav and Xyrem, provides an opportunity for
22 narcolepsy patients to achieve normal sleep architecture
23 which is not a possibility for a patient on those drugs.

24 THE COURT: How do you respond to Jazz's counter
25 to this saying well these were pre-launch statements.

1 MS. DURIE: So they were statements pre-launch
2 that were made by the FDA's sleep experts looking at the
3 clinical trials that had been conducted of these drugs.

4 Now, Jazz has come in here and put up in front
5 of the Court some data about sort of adverse events and
6 things of that nature. The thing THAT I think is most
7 salient about that is what they did not present, which IS
8 the testimony from any medical professional discussing any
9 of that evidence. What the Court heard was pure attorney
10 argument. No indication of how those adverse events
11 compared TO adverse events on Xyrem or Xywav. No testimony
12 from any doctor about how patients experiences on Lumryz
13 compare with their experiences on Xyrem or Xywav.

14 The only evidence on that point before the Court
15 is the evidence that we submitted. It is entirely
16 unrebutted both in terms of medical professionals and in
17 terms of patients. And so I think the Court should take
18 that attorney argument with a grain of salt in view of the
19 fact that Jazz was unable, apparently, to find a single
20 medical professional to submit a declaration to that effect.

21 Just as at trial, Jazz did not offer testimony
22 from any medical doctor rebutting Dr. Korser's testimony
23 about why Lumryz is better for patients. And I want to note
24 here when FDA made this determination on the basis of the
25 data that was generated during the clinical trials, that was

1 a determination made by FDA's sleep experts. Those sleep
2 experts had the benefit of submissions from both Jazz and
3 Avadel, and they concluded on the basis of those submissions
4 and their expert evaluation of it that awakening to take a
5 second dose is not optimally supportive of the continual
6 sleep necessary for narcolepsy patients to restore sleep
7 architecture and daytime alertness with more normal
8 functioning. That is not convenience, that is symptom
9 relief.

10 They further found that awakening to take a
11 second dose necessarily disrupts sleep and causes
12 fragmented sleep. And the problem that is being articulated
13 here is that when your sleep is disrupted, you go,
14 essentially, back to the beginning of sleep cycle. And the
15 problem that FDA is articulating here about stage N3 and
16 disruption of N3, this is a judgment by FDA's sleep experts
17 that having to wake up to take that second dose interferes
18 with the sleep cycle in way that means you never get to the
19 end and get the restorative sleep that you get at the end of
20 sleep cycle, which is a different kind of sleep than you get
21 earlier in the sleep cycle.

22 Again, Jazz has not presented any evidence of
23 any medical professional before this court to contravene
24 that judgment of FDA's sleep experts.

25 And, in fact, what Jazz said when Avadel's

1 product launched was that the approval of another treatment
2 for cataplexy and/or EDS is a positive development for
3 patients with narcolepsy. They said that because that is
4 unambiguously true. It is a positive and I would suggest
5 important development for patients with narcolepsy.

6 Now, we have provided the Court with evidence
7 from medical professionals. We have provided declarations
8 from doctors, including Dr. Ajayi who explains that there
9 had been an underutilization of oxybate when Xyrem and Xywav
10 were the only alternatives. That only about 10 percent of
11 narcolepsy sufferers were taking oxybate therapy and the big
12 reason for that was the twice-nightly dosing regimen. And
13 that for that reason Lumryz is expanding the number of
14 narcolepsy sufferers who can have the benefit of oxybate
15 therapy. Now that is not only Dr. Ajayi's opinion.

16 In Jazz's open brief, Jazz said that Avadel
17 cannot show that the injunction seeks to limit access to
18 Lumryz to patients who cannot be helped by Jazz's products.
19 But that is in fact exactly what the evidence shows. It
20 shows it from their own expert because we asked Dr. Rainey
21 at trial whether he agreed that Lumryz was being used by
22 patients who would not otherwise be taking Xyrem or Xywav,
23 and he agreed that is part of the Lumryz patient population.
24 And he agreed because that is true.

25 Now, again, Jazz bears the burden on this point.

1 We presented the evidence of medical professionals. They
2 presented nothing to counter this. And what we see in
3 Dr. Stern's declaration is that the improvements that we
4 see -- it's not just convenience. The improvements in
5 patient compliance, which is to say many patients can't wake
6 up to take the second dose, but with Lumryz they don't need
7 to so they are more likely to get the full benefit of the
8 therapy, that leads to better outcomes, both in terms of
9 symptom control and quality of life. Again, un rebutted
10 testimony.

11 We also provided the Courts with declarations
12 from a number of patients. These are patients who are
13 attesting to their experience.

14 Now, I heard counsel suggest that, you know,
15 maybe patients shouldn't be trusted to report on their own
16 experience, but I would say in reading these declarations
17 these patients are clear and specific about why they have
18 benefited from Lumryz relative to Xyrem or Xywav and what a
19 powerful impact that has had. Including the fact that in
20 this case a student who had problems not missing class on
21 prior therapy and has seen a big difference after switching
22 to Lumryz. That includes patient two who had negative
23 experiences on Xywav and then started Lumryz and had a much
24 more positive experience. The days were more consistent
25 because sleep was more consistent.

1 Patient three who, as a consequence of improved
2 sleep, is now able to keep a consistent schedule,
3 concentrate better and hold down a job. That includes
4 patient S who talked about the fact that they are now --
5 that patient is now getting the best quality of sleep, in
6 their judgment, that is possible and that their quality of
7 life has improved.

8 And patient F who is a teacher who talked about
9 the problems that she had taking Xyrem and Xywav, that there
10 was the problem with waking up but not being able to take
11 the second dose, sleeping through the alarm and that this
12 patient has found Lumryz has allowed them to stay asleep all
13 through the night. And that when they were on Xyrem or
14 Xywav not only would they wake up in the night, but they
15 would have these nighttime events; in this case eating in
16 the middle of the night that caused weight gain and made
17 them feel terrible.

18 Now, I want to be clear the only medical
19 evidence we have from any Jazz-affiliated doctor on this
20 point is what Dr. Bogan said at his deposition. And what he
21 said at his deposition in this case, Jazz's expert, is that
22 as a clinician he would like to have once-nightly oxybate
23 available.

24 The evidence that we have put in on this point
25 is substantial, that doctors and patients see important

1 benefits, not merely convenience, but important benefits in
2 terms of symptom control, the ability to hold down a job,
3 the ability to go to classes as a function of being able to
4 sleep through the night due to Lumryz.

5 And, again, I want to note that everything that
6 you heard that counters this evidence is attorney argument
7 because Jazz put in no evidence to meet its burden on this
8 point.

9 Now, we had discussion about sodium-sensitive
10 patients. And what I want to note with respect to
11 sodium-sensitive patients is -- I heard, I think, a
12 statement that FDA found that sodium-sensitive patients
13 should be on Xywav. If I heard that correctly, that is not
14 what FDA found. What FDA said is that although it is widely
15 accepted that everyone should limit sodium intake generally,
16 the warning on Lumryz's labeling regarding sodium is
17 directly only at patients sensitive to sodium intake, such
18 as those with heart failure, hypertension and renal
19 impairment. And then with respect to those patients what
20 FDA found is for certain sodium-sensitive patients with
21 narcolepsy, the benefit offered by once-nightly dosing would
22 outweigh the risk of increased sodium intake for reasons; in
23 other words, having to wake up to take the second dose is
24 antithetical to oxybate's goal on improving sleep,
25 disrupting sleep contributes to chronic sleep loss, etc.,

1 with detrimental effects on both psychological and physical
2 health, and there are other ways such patients may reduce
3 such sodium in their diet. So there is a clear benefit for
4 many patients whether sodium-sensitive or not to Lumryz.

5 Now, Jazz has tried to avoid, I think, the force
6 of this evidence by suggesting that they are only seeking a
7 limited injunction. First point I want to make there was is
8 no reason that patients who are not yet on Lumryz are any
9 less deserving of those benefits than patients who already
10 have been prescribed the drug. And we put in in a
11 declaration from Dr. Stern an explanation of who those
12 patients are. Some of them haven't yet been diagnosed with
13 narcolepsy. Some of them may not yet have gotten insurance
14 coverage to take Lumryz. Some of them may not yet be 18.
15 Some of them not yet completed the process of going through
16 the risk, the REMS for Lumryz, the Risk Evaluation and
17 Mitigation System. There are many reasons that patients may
18 not yet be on Lumryz, but still benefit from it, and those
19 patients are every bit deserving of the benefit.

20 Indeed, Nurse Practitioner Maggie Lavender put
21 in a declaration explaining that she has patients who she
22 can't get prescribed Lumryz, but she wants to; and that she
23 expects that those patients will benefit from it when it is
24 available for them, including in this example a patient who
25 has parasomnia symptoms, this twilight mode where you're

1 sort of half awake and half asleep on Xywav. And actually
 2 in one instance when he was in college, the patient drove to
 3 a store and caused a disturbance in the middle of night not
 4 being aware that they were in this parasomnia state, and
 5 this is a really serious issue. This patient deserves
 6 access to Lumryz and deserves it every bit as much as the
 7 patients who were currently on it.

8 Now, although Jazz has tried to suggest that the
 9 injunctions that they seek are limited, we have put in
 10 evidence that even a limited injunction is, in effect, an
 11 injunction for everyone. Avadel is a one product company.
 12 Now, there's been a suggestion that's Avadel's own fault.
 13 I'm going to talk about that, but the point I want to make
 14 right now is whatever it is or isn't, it's not the patient's
 15 fault. I'm talking right now about public benefit. And
 16 from a public benefit point of view no patients will get
 17 this benefit if there is an injunction that precludes Avadel
 18 from being able to serve future patients.

19 THE COURT: Well, let me ask you --

20 MS. DURIE: Yes.

21 THE COURT: -- the same question I asked

22 Mr. Cerrito: From a you public interest perspective, isn't
 23 there a difference between narcolepsy and IH?

24 MS. DURIE: I'm glad that the Court asked that
 25 because I was about to talk about IH. And the answer is

1 there is a difference, but there is a strong public benefit
 2 with respect to idiopathic hypersomnia too.

3 I think the most critical fact here is that
 4 although Jazz's counsel says that Xywav is approved for
 5 once-nightly, the evidence is that only about a quarter of
 6 patients with idiopathic hypersomnia are taking Xywav
 7 once-nightly and a quarter of it are taking twice-nightly,
 8 and the reason for that --

9 THE COURT: Even more basic than that because
 10 public interest is two factors, okay. You've got to public
 11 interest in protecting intellectual property, which, you
 12 know, encourages innovation; and then you've got the public
 13 interest in having access to the drugs. But one of the
 14 distinctions -- is there a distinction here between
 15 narcolepsy -- when it comes to access to the drugs, is there
 16 a distinction between narcolepsy, which is with respect to
 17 narcolepsy, there's been -- the FDA has said that Lumryz has
 18 some clinical superiority.

19 MS. DURIE: Correct.

20 THE COURT: But it hasn't done that with respect
 21 to IH.

22 MS. DURIE: Not yet. And the reason for the
 23 "not yet" is that Avadel has not yet done the clinical trial
 24 that would result in presenting that question to FDA.

25 THE COURT: Okay.

1 MS. DURIE: And one thing I want to note off the
 2 bat, Avadel is not engaging in any infringing conduct with
 3 respect to IH. Right now Avadel is selling Lumryz with a
 4 label for narcolepsy.

5 Your Honor referred to off-label usage. There
 6 is some, we don't promote it, we don't control it, we don't
 7 have anything to do with it, we're not allowed to. That is
 8 a judgment being made by an individual doctor about whether
 9 they're going to prescribe Lumryz for their IH patient. We
 10 don't do anything to encourage that.

11 And as the evidence shows, it's a very small
 12 number of patients. I think it's eleven patients, probably
 13 because there's no insurance coverage for it in that
 14 scenario.

15 Avadel has not yet started a clinical trial for
 16 idiopathic hypersomnia, it intends to. It intends to invest
 17 \$35-40 million in that clinical trial. That clinical trial
 18 will fall within the FDA's safe harbor. That is infringing
 19 activity because we have made a policy judgment that we
 20 companies to conduct those clinical trials, regardless of
 21 issues with respect to patent infringement.

22 After that clinical trial has been done, Avadel
 23 will make a submission to FDA and FDA will then have an
 24 opportunity to evaluate whether Lumryz makes the same major
 25 contribution to patient care in idiopathic hypersomnia as it

1 does in narcolepsy.

2 Now, we have put in evidence as to why we think
 3 the answer to that question will be yes, and that is because
 4 we expect it to have the same benefit because most
 5 idiopathic hypersomnia patients take Xywav or Xyrem
 6 twice-nightly, and we think they will see the same benefits
 7 on Lumryz of being able to take a single dose and sleep
 8 through the night.

9 THE COURT: Okay. But infringement of Claims 14
 10 and 24, it's been said that Avadel doesn't currently do
 11 anything that infringes the patent. And one of the things
 12 that Jazz is asking for is a permanent injunction with
 13 regard to that. So if the Court granted the permanent
 14 injunction with respect to IH, that wouldn't put Jazz --
 15 that wouldn't put Avadel out of business, right, because you
 16 aren't doing anything?

17 MS. DURIE: Well, I don't think that's
 18 necessarily correct. Avadel operates at a very substantial
 19 loss right now. It made huge investments in Lumryz well
 20 before it knew about Claim 24 of the patent or could have
 21 known. It made huge investments in clinical trials to bring
 22 a product to market with the hope that it would be able to
 23 recoup those expenses and then be able to continue to sell
 24 that product in a profitable way.

25 So actually Avadel does depend upon the ability

1 to grow and expand its business, that's part of the point of
 2 Mr. Divis' declaration, generally, in order to be able to
 3 continue to sell Lumryz. But I want to make sort of a
 4 fundamental point here: Yes, Jazz is asking for a permanent
 5 injunction. Nothing that Avadel will do would be subject to
 6 an injunction for a very long period of time, because Avadel
 7 can't infringe right now; it does haven't a FDA approval to
 8 sell a product and it won't have that FDA approval for years
 9 in the future. I think the estimate was something like
 10 three or four years, something on that order of magnitude.
 11 That is the first point of time at which there would even be
 12 a question about whether Avadel sales should be enjoined for
 13 idiopathic hypersomnia, because before then Avadel would not
 14 be infringing, it would be operating within this regulatory
 15 safe harbor that allows for conduct that would otherwise
 16 infringe if that conduct is intended to generate data for
 17 submission to FDA.

18 And, again, we have -- there's a reason that
 19 companies cannot infringe patents when they are conducting
 20 clinical trials that is because we want to encourage
 21 companies to do that. And we want to encourage companies to
 22 do that in order to generate the data that the Court would
 23 then be able to look at --

24 THE COURT: Right, but that's protected by
 25 statute --

1 MS. DURIE: That's protected by statute, that's
 2 exactly right.

3 At that point FDA will look at the data and make
 4 a decision about whether Lumryz offers a major contribution
 5 to patient care.

6 Now, again, Jazz bears the burden on this point.
 7 Jazz has put in, I will say, evidence about Xywav -- and I
 8 will talk about that -- but we have put in evidence from
 9 medical professionals explaining why there is a need now for
 10 patients with idiopathic hypersomnia for Lumryz and,
 11 therefore, why we expect that FDA is going to reach the same
 12 conclusion at the conclusion of those clinical trials.

13 So the first point most idiopathic hypersomnia
 14 patients take Xywav twice a night. On the label it says
 15 once a night or twice a night, most patients take it twice a
 16 night. So we put that in, that's evidence from Dr. Stern,
 17 that's in the declaration from Nurse Practice Maggie
 18 Lavender. This is not merely anecdotal evidence, although
 19 it is the only evidence from any medical professional on
 20 this. This is entirely unsurprising because this is what
 21 was reflected in the clinical trial for Xywav.

22 Now, on the Xywav label it says that in the
 23 clinical trial 23 percent of patients took Xywav
 24 once-nightly with a median dose of 4.5 grams and 77 percent
 25 of patients took it twice-nightly with a median dose of

1 7.5 grams. I want to explain how this clinical trial was
 2 structured because it's a little bit unusual.
 3 Patients and their doctors were given the
 4 opportunity to identify to select the dosing regimen that
 5 they would be on, the one that as between these two Xywav
 6 options was credible or least bad for them. And as a result
 7 of those individualized decisions between doctors and
 8 patients, 77 percent of patients wound up taking Xywav
 9 twice-nightly. Then in the clinical trial aspect, half of
 10 those patients stayed on that drug at the dose and the
 11 dosing schedule that they had selected. The other half were
 12 switched to a placebo. And in the study what they evaluated
 13 was how much better patients did when they stayed on drug
 14 relative to what happened when they switched to a placebo.

15 But the thing that's critical about this is
 16 three-quarters -- more than three quarters of patents were
 17 taking it twice-nightly, which makes it entirely
 18 unsurprising the evidence we put in from doctors and from
 19 Nurse Practitioner Lavender is consistent with that.

20 So why is that if patients want to be able to
 21 sleep through the night? There are a number of reasons, but
 22 one of them has to do with dose. Xywav is an immediate
 23 release product. All of the drug that you take is
 24 immediately going to hit your system. For that reason, the
 25 maximum dose of Xywav that you can take at once is 6 grams,

1 because it isn't safe to have more than 6 grams hit your
 2 system at once. So if you are a patient who needs more than
 3 6 grams of oxybate in order to get sleep, you're not going
 4 to get that with the once-nightly dose of Xywav.

5 Lumryz, by contrast, can be dosed up to 9 grams,
 6 and that's because you have that two-phase release, half of
 7 it releasing right away, half of it releasing later so it's
 8 safe for you to take a higher dose. And what we saw here on
 9 the Xywav label 77 percent of patients were taking Xywav
 10 twice-nightly median nightly dose of 7.5 grams, that's more
 11 drug, which presumably they and their physician determined
 12 that they needed than it would be possible for them to get
 13 if they were taking Xywav once-nightly.

14 THE COURT: Well, doesn't that also support the
 15 causal nexus because that's the invention of Claim 24, the
 16 immediate release and the modified release?

17 MS. DURIE: So both immediate release and
 18 modified release are elements of the claim, I agree with
 19 that. However, at trial, Jazz said with respect --
 20 immediate release was in the prior art, everybody agrees
 21 with that.

22 At trial Jazz said "modified release was in the
 23 prior art." And it pointed to its earlier prior art
 24 disclosure of modified release in the '488 patent as
 25 providing the support for that for Claim 24.

1 What Jazz said was not in the prior art, what it
2 said it had added was this idea of a thickener of a separate
3 acid and of putting it into a sachet. Now I'll talk about
4 that more in a minute, but I think the fundamental point for
5 what did Jazz contribute, those are the things that it
6 contributed in Claim 24; not the ability to have
7 once-nightly dosing.

8 And in fact, as we'll see, Jazz was very clear
9 with Your Honor that Claim 24 was not about once-nightly
10 dosing. They didn't invent it. They couldn't do it. They
11 didn't need to be able to do it because that's not what
12 Claim 24 was about. The reason patients are taking Lumryz
13 is because of once-nightly dosing; it's because it allows
14 them to get all of the drug they need once at bedtime and be
15 able to sleep through the night.

16 And certainly with respect to public benefit for
17 idiopathic hypersomnia, the 77 percent of patients or so who
18 cannot take Xywav once-nightly because it doesn't provide
19 enough drug for them, who currently are taking it
20 twice-nightly just as with narcolepsy and are suffering all
21 the burdens that FDA ascribed to twice-nightly dosing and to
22 having to wake up in the middle of the night, those patients
23 are equally deserving of Lumryz. That's why Avadel is
24 willing to invest \$35-40 million dollars in a clinical trial
25 to prove those benefits to FDA.

1 Now, I want to say, what I just explained is
2 articulated in Dr. Stern's declaration. He talks about the
3 maximum dose of Xywav being 6 grams as compared to 9 grams
4 for Lumryz and why that means that many patients, in fact
5 most patients, cannot get full symptom relief by taking
6 Xywav once-nightly and why in his opinion Lumryz is going to
7 be better for those IH patients in the same way that it has
8 been determined to be better for patients with narcolepsy.

9 And we put before the Court Greg Davis'
10 declaration explaining that the reason that Avadel is
11 proposing to do this trial is because physicians and the
12 sleep disorder community have been urging it to do so
13 because of the benefits that they expect will accrue from
14 being able to use Lumryz for idiopathic hypersomnia
15 patients.

16 Now, in substance, what the evidence shows is
17 that there may be 23 percent of patients, up to 23 percent
18 of patients who are doing okay on once-nightly Xywav, and
19 that's fine. But here the question is whether there is a
20 patient population who will benefit substantially from
21 having Lumryz available. It doesn't need to be all
22 patients, it is sufficient if it be some patients. And if
23 one device is more suitable for some patients and another
24 device is more suitable for other patients, that is the
25 circumstance where patients should have that choice; that's

1 what the Court found in *Abbott v. Edwards Life Sciences*, and
2 that's what is true here because we have these very
3 differentiated products. And there are patients who need
4 more than 6 grams of oxybate, need a second dose in the
5 middle of the night and should be able to get the same
6 life-changing benefits of that therapy in.

7 Now, I want to note that Jazz submitted some
8 declarations in connection with its reply brief. It
9 submitted a declaration from Dr. Kryger. He did not rebut
10 any of the things that I just said. And I think it's
11 telling that they chose to put before the Court a
12 declaration from someone who is absolutely and without
13 question is a sleep expert. What did he say? Idiopathic
14 hypersomnia and narcolepsy are not the same condition.
15 That's fine. We're not saying they are the same condition.
16 They exist on a spectrum. Patients are sometimes diagnosed
17 with idiopathic hypersomnia and then rediagnosed with
18 narcolepsy. But it doesn't matter because the point that
19 matters is that oxybate is a highly effective treatment for
20 idiopathic hypersomnia. He doesn't disagree with that.

21 He also says idiopathic hypersomnia is
22 characterized by sleep inertia where the patient wakes up
23 irritable or very drowsy, that it is really hard to wake up.
24 That's true. That's what Dr. Stern explained that it's even
25 harder for IH patients to wake up for that second dose when

1 they need that additional drug, and why it's even more
2 important for them to have a drug that they can take once at
3 bedtime and sleep through the night. Dr. Kryger doesn't
4 disagree with that.

5 And finally he said narcolepsy is characterized
6 in many cases by disrupted nighttime sleep, but that's not
7 typically seen in idiopathic hypersomnia. Same point. I
8 think if anything that supports our position. And, in fact,
9 what is shown in the documents associated with the Xywav
10 label is that patients were considered for twice-nightly
11 dosing if they reported disruptive nighttime sleep or
12 difficulty with sleep maintenance, and we know that was
13 77 percent of the patent population.

14 And, in fact, previously in a letter that he
15 submitted to FDA, Dr. Kryger surveyed the treatment
16 landscape at that point in time, which is to say
17 twice-nightly doses, said that patients having to awaken in
18 the middle of the night to take a second dose was an issue,
19 and described this as a cumbersome treatment that had not
20 changed in about 40 years. So we can understand why it is
21 that they did not have Dr. Kryger articulate his views
22 responsive to the medical testimony that we put in.

23 Now, I want to note that there was a suggestion
24 in the reply papers that Xywav once-nightly is sort of
25 equivalent to Xywav twice-nightly at least for the

1 23 percent of patient who is are on a once-nightly regimen.
 2 This is the actual data, and I want to note here this is
 3 from the Xywav approval package, Figure 5. And what it's
 4 showing here is the range of the sort of median and then the
 5 range of sort of outcomes from a statistical point of view
 6 for the once-nightly treatment and the twice-nightly
 7 treatment. The score that goes from zero to negative-11 is
 8 the Epworth sleepiness scale. And what is this is showing
 9 is how much better patients did or how much worse patients
 10 did when they went off drug or how much better they did when
 11 they stayed on drug, but the bigger the negative number the
 12 bigger the impact when they switched to placebo.

13 So a more negative number is the drug was more
 14 effective because there was a bigger effect, a bigger
 15 worsening of symptoms when they switched to a placebo. You
 16 see the numbers that are reported by Jazz about minus-3,
 17 which is a pretty big band for once-nightly, maybe minus-7.5
 18 with a slightly smaller band, but still a significant one
 19 for twice-nightly. That's the data. This is something Jazz
 20 put in their reply brief. For that reason we don't have a
 21 declaration responding to it, but I would just note that
 22 that data looks pretty different in terms of the
 23 effectiveness of the once-nightly and the twice-nightly
 24 Xywav regimens for idiopathic hypersomnia.

25 The fundamental point here, Your Honor, with

1 respect to idiopathic hypersomnia is that Jazz has not met
 2 its burden, and it is its burden to show that these patients
 3 would not benefit and that there is, for that reason, a
 4 public benefit in precluding them from having access to this
 5 potentially life-changing treatment.

6 And in the *United Therapeutics* case the Court
 7 there found where at least some patients would likely suffer
 8 negative consequences that was a reason to conclude that the
 9 plaintiff has failed to do show that an injunction would be
 10 in the public interest. And I would suggest here we have
 11 put in a great deal of evidence about why we plan to invest
 12 money in a clinical trial and what we expect FDA's
 13 determination will be, why we expect they will reach the
 14 same conclusion, and essentially un rebutted evidence from
 15 medical practitioners about why it makes sense.

16 THE COURT: But isn't the difference here -- so
 17 you said yourself, as of today there's a very small number
 18 of patients that have -- that suffer from IH that have even
 19 been prescribed Lumryz.

20 MS. DURIE: That is true.

21 THE COURT: Right. And what was that number
 22 again?

23 MS. DURIE: I believe it's 11.

24 THE COURT: Eleven. All right. So in these
 25 cases where, you know, the differentiator of the product is

1 the basis to deny the permanent injunction the product has
 2 actually been prescribed, right?
 3 MS. DURIE: No. And actually this *United*
 4 *Therapeutics* case is interesting because this was about
 5 whether defendant should be enjoined from launching the
 6 product for a particular medication. So there the product
 7 had not launched, and the Court said I'm not going to enjoin
 8 the product from launching because I think doing so would
 9 mean that patients would likely suffer negative consequences
 10 if that product didn't launch.

11 The point here, Your Honor -- I mean, it's true
 12 Avadel has not yet done the clinical trial. Part of why
 13 Avadel didn't do the clinical trial yet was because of
 14 Jazz's conduct which kept it off the market as a function of
 15 the REMS patent and delayed the launch of Lumryz itself for
 16 narcolepsy. But be that as it may -- and I'll talk more
 17 about that, but be that as it may, the fundamental point
 18 idiopathic hypersomnia patients deserve access to the drug
 19 that is best for them just as narcolepsy patients do.

20 The timing of the clinical trials is not
 21 relevant to their need. So the only question should be have
 22 we -- has Jazz shown, has Jazz met its burden to show that
 23 the health of those patients will not be adversely impacted
 24 if the Court enters an injunction.

25 THE COURT: That's not the only question. The

1 question is does -- will the permanent injunction disserve
 2 the public interest. And, again, the public interest is two
 3 factors: The protection of intellectual property rights and
 4 then the accompanying healthcare benefits of patients. And
 5 so that's -- you know, the Court has to look at both of
 6 those factors and factor that in. And so that's sort of the
 7 state of -- sort of the use of the drug is different for
 8 narcolepsy as it is for IH.

9 MS. DURIE: Not in a way that I think is germane
 10 to the decision the Court needs to make. It is true in
 11 every case that there's a public interest in patent rights.
 12 What the Court's have said is we're not going to permanently
 13 enjoin activities that would injure the public health, that
 14 the public health is sacrosanct. Again, where there is a
 15 differentiated impact that is a true public health impact.

16 So the timing and sort of what the status quo
 17 is, I don't think is relevant to that public health
 18 determination. The question is: Are those patients likely
 19 to receive the same benefit? And, again, I want to note
 20 there's nothing to enjoin now. We're not doing anything in
 21 idiopathic hypersomnia to infringe. We need to run a
 22 clinical trial. There's nothing to enjoin with respect to
 23 the clinical trial, that's not infringing.

24 At that point, FDA will look at the data and
 25 will make a decision. At that point, I suppose, maybe Jazz

1 could come back and say now we want an injunction because we
2 don't think there's any benefit to public health and we
3 could make a showing, maybe they could make a showing then
4 that they are unable to make now. But I would say on this
5 record, they have not made any showing that should cause
6 this court to prejudge what determination FDA is going to
7 make once the clinical trial is done and once FDA has the
8 benefit of looking at that evidence to see what the benefits
9 to idiopathic hypersomnia patients will be. And I think the
10 public health benefit, from a public health point of view is
11 what is best for patients. It doesn't matter whether the
12 therapy is already on the market or not. The goal is to
13 make sure that patients can have the therapy that is best
14 for them.

15 THE COURT: But if a competitor can, at any
16 time, just come in to court and say well, you know, we're
17 going -- we are coming up with a competitive drug that
18 infringes Company A's patent, but our drug is going to have
19 some differentiating feature that is going to more benefit
20 patients, if that -- and it doesn't matter whether that drug
21 was in the market being currently prescribed and would be
22 being taken away from patients as opposed to a drug that's
23 been in the market, has been prescribed to patients, you
24 know, if you don't put some limit on it at some point then
25 that's just opening the door for infringement.

1 MS. DURIE: No, Your Honor. And, one, I would
2 say there is no injunction factor that looks at whether the
3 product is already on the market; that's not one of the
4 injunction considerations in the permanent injunction
5 context that we have been looking at. It is -- in terms of
6 a preliminary injunction, status quo can matter in terms of
7 determining the status quo, but here the test is public
8 interest not maintaining the status quo.

9 THE COURT: Right. Public interest, and public
10 interest includes protecting intellectual property right --

11 MS. DURIE: It absolutely does. But I would
12 say, Your Honor, this is why in part we have that regulatory
13 safe harbor. We want companies to conduct the clinical
14 trials in order to develop the evidence that then allows the
15 Court to evaluate, at the point of launch, which is when
16 that is typically going to happen, whether there is a public
17 benefit in allowing the launch and allowing the product to
18 come on the market.

19 And, bear in mind, we have a safe harbor,
20 statutory safe harbor for the clinical trial, you're not
21 infringing. We then also, when there are Orange Book listed
22 patents, as the Court knows, we have an automatic stay. The
23 purpose of that automatic stay is to allow the patent
24 infringement issues to be adjudicated before launch. And
25 the point of that is to give the Court the ability both to

1 have the benefits of the clinical trials and see what the
2 evidence is with respect to patient benefit and to be able
3 to make a determination before launch about whether that
4 launch should happen.

5 In that context the Courts look at the public
6 health and make a determination about whether the product
7 should be permitted to launch or should not be permitted to
8 launch, based on the showing with respect to all four of the
9 injunction factors, but, for this case critically, the
10 public health, public benefit factor and whether the public
11 benefit is going to be served by that launch.

12 Again, I think the reason that it is set up that
13 way is precisely because we don't want patients to suffer
14 just by the happenstance of when it is that companies
15 conducted clinical trials for particular indications. We've
16 seen -- and the Court has evidence about -- just how
17 important and beneficial Lumryz is for narcolepsy patients.
18 If idiopathic hypersomnia patients get that same benefit, as
19 we expect them to do, a benefit that allows them to hold
20 down a job, allows them to go to classes, allows them not to
21 drive around unsafely in the middle of the night, they
22 should have those public health benefits too.

23 THE COURT: Let me ask you this question: Does
24 Avadel have noninfringing alternatives of Lumryz available?

25 MS. DURIE: That is an excellent question and

1 there are two things I want to say about that: First, I
2 would note, at trial Jazz argued over and over and over
3 again that there is no noninfringing alternative. Their
4 experts said that over and over, and that was part of
5 Dr. Rainey's damage opinion that there was no noninfringing
6 alternative, no noninfringing alternative.

7 Two, this is an -- this situation -- we're not
8 selling a nail where you can just change the nail and all of
9 a sudden not infringe. The problem here is the need to get
10 regulatory approval, so we can't just change our product and
11 start selling it. Jazz had to make all of its product
12 decisions, conduct clinical trials with that product, get
13 that product approved by FDA and that is the product that we
14 have approval from FDA to sell. So the answer is this is
15 what is called sometimes regulatory lockup or regulatory
16 holdup because we, as a practical matter, can't just make a
17 change to the product and start selling it without going to
18 FDA and without dealing with regulatory approval.

19 So Avadel made all of the decisions about what
20 its product was going to be before it knew about Claim 24;
21 in fact, before Jazz had applied for Claim 24. At the point
22 in time where Avadel made all of those decisions, Claim 24
23 didn't exist, the application didn't exist. Avadel had no
24 way to know that Jazz was going to claim that this was its
25 intellectual property. And it made all of those investments

1 at that period of time leading up to FDA approval in good
2 faith and invested \$150 million in getting that regulatory
3 approval to be able to bring this product to market.
4 So when Jazz says well, you should just switch,
5 what Jazz is really saying is scrap all of that, go back and
6 start all over again, reformulate a product, redevelop a
7 product, do whatever you need to do, go back to FDA do
8 whatever FDA says you need to do and then maybe some day FDA
9 will let you come out with a different product. So that is
10 why there is this notion of regulatory holdup or regulatory
11 lockup, and I will -- when we get there, there's a case that
12 considered this precise question and found that is a
13 situation that weighs against entry of an injunction. Note:
14 Jazz could have sought this claim back in 2016, it chose not
15 to. Had Jazz done that in 2016 and allowed the fact of that
16 claim to publish, we would have been on notice that this is
17 something that Jazz claimed was its intellectual property
18 and we could have conducted ourselves accordingly. Jazz
19 didn't do that.
20 Jazz waited to file this claim until after they
21 saw our patent application, as the Court knows, and even
22 then Jazz kept that claim a secret from us until the day
23 they sued us. So Jazz affirmatively tried to prevent Avadel
24 from learning about this intellectual property so that
25 Avadel could continue -- would continue down the path that

1 it was on and would not make changes. So for Jazz now to
2 come into court and say that we acted at our peril when Jazz
3 kept from us any information about their intellectual
4 property is, I would suggest, a little rich.
5 Avadel made its investments in good faith. It
6 spend a lot of money to bring this product to patients and
7 it did so with absolutely no way of knowing that Jazz later
8 was going to claim something that it owned.
9 THE COURT: All right.
10 MS. DURIE: Now, I want to move on to the other
11 factors. I want to touch briefly on balance of hardships.
12 So with respect to balance of hardships, the Court can
13 consider a number of things: The party sizes, their
14 products and their revenue sources. This is, again, one
15 respect in which this case is different from *Natera* because
16 in *Natera* the Court found that revenues from the product at
17 issue were a small fraction of Invitae's business. Here
18 Lumryz is our only product and we've put forward evidence
19 that an injunction would bankrupt Avadel.
20 Now, just before I move on, I want to note,
21 again, Jazz's argument is well, you brought this on
22 yourselves. We didn't. At the point in time that we
23 investigated \$150 million we had no way to know about
24 Claim 24. At the point when Avadel became a one-product
25 company and said we need to provide this product to patents,

1 we need to put all of our resources into this product, that
2 was in 2019, that was before Jazz even filed for Claim 24;
3 so all of those decisions were already baked and it had
4 already been made. And the consequence of that and Jazz not
5 discussing the fact that it owned this intellectual property
6 is that Avadel finds itself in this situation where it would
7 be bankrupted.
8 Jazz, on the other hand, has said repeatedly in
9 public statements, on earnings calls that have to be
10 accurate as a matters of SCC rules, that notwithstanding
11 competition from our product, it expects Xywav to remain the
12 oxybate of choice, including the number one treatment for
13 narcolepsy. Jazz has said it's confident in durability of
14 Xywav. That it's well-positioned to achieve its goal of two
15 billion in sleep revenue in 2025. That Xywav's revenues
16 increase 14 percent year-over-year, notwithstanding
17 competition from Lumryz, reenforcing its confidence, its
18 trajectory and durability. What we are talking about on
19 Avadel's side is bankruptcy. What we're talking about on
20 the Jazz side it is maybe instead of increasing 14 percent
21 year-over-year it would increase 17 percent or some -- but
22 that's what we're talking about when we're talk about the
23 harm on the Jazz side of the ledger. Now I said we made
24 these investments in good faith.
25 In the *Hynix* case, the Court considered a

1 related kind of lock-in. Now there it wasn't regulatory
2 lock-in from FDA, it was lock-in from being part of a
3 standards essential group with a standards essential patent.
4 But the point was the same. The point said -- the Court
5 said: Sure, generally if you elect to build a business on a
6 product found to infringe, you can't be heard to complain
7 about that. But the Court said this was a different
8 situation because there was a lock-in and that lock-in
9 resulted from the fact that Rambus didn't disclose and in
10 fact didn't obtain the patents until after, in that case, it
11 had established RDRAM as an industry standard. Here it's a
12 similar thing; in that, Jazz did not disclose or in fact
13 obtain the patents-in-suit until after Avadel had made all
14 of its investments in getting regulatory approval for
15 Lumryz.
16 THE COURT: But, again, when you say there's --
17 the situation that Avadel is facing is bankruptcy, I get it
18 with respect to narcolepsy. But with respect to IH
19 that's -- that can't be true because you're not in that
20 market substantially.
21 MS. DURIE: So --
22 THE COURT: And if you weren't allowed to
23 infringe their patent with respect to IH, then the money you
24 would spend on the FDA you would save.
25 MS. DURIE: So -- well, so it is true that if

1 the Court were to decide now that no matter what benefits
 2 FDA found for idiopathic hypersomnia patients, regardless of
 3 the patient benefit it didn't matter and said now no matter
 4 what FDA finds we're going to injoin sales of IH at the
 5 conclusion of the clinical trials, so three or four years
 6 from now, I think it's probably true that Avadel wouldn't
 7 run a clinical trial if there was no way that it could sell
 8 product at the conclusion of that clinical trial. Although,
 9 I would suggest there's no reason for the Court to make that
 10 judgment now, rather than waiting to see what the result of
 11 the clinical trial is and what the evidence actually is with
 12 respect to patient benefit at that point in time. That
 13 doesn't mean, though, that Avadel can be successful only in
 14 the narcolepsy market. It's true that right now Avadel only
 15 sells in narcolepsy. Right now Avadel loses money. Avadel
 16 made a massive investment in developing Lumryz, totally in
 17 good faith with no reason to know anything about Claim 24 of
 18 the '782 patent, with the expectation that it would be able
 19 to bring that product to market for the range of patients
 20 who need it, including patients with idiopathic hypersomnia.
 21 So I don't think the Court can conclude Avadel will be fine
 22 if it is limited to the market for narcolepsy patients.
 23 But my other main point, Your Honor, would just
 24 be right now there is no basis for the Court to find that
 25 the public health concerns with respect to idiopathic

1 hypersomnia are any different than they are for narcolepsy.
 2 Jazz's arguments was well we've got once-nightly dosing for
 3 Xywav, that's 21 percent of patients. For the other
 4 77 percent of patients, they're in the same situation as
 5 narcolepsy patients.
 6 So I would say if the Court -- we think that we
 7 have made a sufficient showing today with respect to those
 8 patients, but if the Court disagrees the right thing to do
 9 is to wait. Let us run a clinical trial, which does not
 10 infringe. Let us present the results of that clinical trial
 11 to FDA, which does not infringe. Let FDA make a judgment,
 12 as they did with narcolepsy, about what the benefits are.
 13 At that point the Court would have a record and Jazz could
 14 make an argument that the evidence for idiopathic
 15 hypersomnia is different than for narcolepsy. It is
 16 different, we don't think it is going to be, but we -- I
 17 mean, we can't definitively -- right now we've got doctors
 18 put in front of you saying we expect those patients will get
 19 the same benefits.
 20 At a minimum, if the Court doesn't find the
 21 declarations of those doctors saying we've got idiopathic
 22 hypersomnia patients, they're suffering, we expect them to
 23 get the same benefits; if that's not sufficiently
 24 compelling, then wait until we develop the evidence and FDA
 25 has an opportunity and the experts at FDA have an

1 opportunity to look at that evidence to see what the
 2 magnitude of that benefit really is before the Court
 3 concludes that idiopathic hypersomnia patients don't deserve
 4 access to that therapy.
 5 THE COURT: I understand your argument.
 6 MS. DURIE: And so the point here, Your Honor,
 7 is simply that Jazz should not be permitted to suggest
 8 credibly that it is Avadel's fault, that Avadel made these
 9 investments when Avadel had no way of knowing that Jazz was
 10 seeking this patent protection. And, in fact, the original
 11 date where FDA was anticipating approval, October 15th of
 12 2021, was before the '782 patent even issued. We'll get to
 13 this, but had it not been for the whole REMS patent
 14 situation, we might well have been on the market with
 15 respect to narcolepsy and beginning clinical trials of
 16 idiopathic hypersomnia before the '782 patent was even made
 17 known to us.
 18 THE COURT: Right. So the FDA process that was
 19 going on during the time that '782 patent was not public had
 20 to do with narcolepsy?
 21 MS. DURIE: Correct. That's correct. We had
 22 not yet commenced a clinical trial in idiopathic hypersomnia
 23 because we were waiting for FDA's determination with respect
 24 to narcolepsy, which was supposed to come out in October of
 25 2021, but didn't actually come out until 2023 because of the

1 Orange Book listing issue of which the Court, I know, is
 2 well aware.
 3 So in short, with respect to the balance of
 4 hardship, we think this factor also is in Avadel's favor,
 5 because we made our investment in good faith before we could
 6 possibly know about the existence of Jazz's patent
 7 application; because an injunction would bankrupt a company
 8 that engaged in that good faith conduct; and because Jazz in
 9 its own words expects that it will continue to be
 10 successful, notwithstanding competition from Avadel.
 11 I want to turn next to irreparable harm, which,
 12 as the Court has noted, is a closely related factor. First
 13 point I want to make is that the Federal Circuit -- and this
 14 is from a District Court case citing the Federal Circuit in
 15 *Automated Merchandising*. The Federal Circuit has found that
 16 lost sales standing alone are insufficient to prove
 17 irreparable harm, because if that was enough there would be
 18 irreparable harm in every case. So it is a factor, but it
 19 is not sufficient. And Courts in this district and the
 20 District of Delaware have also found that courts have
 21 routinely decided that market share and price erosion do not
 22 amount to irreparable harm. That's not sufficient either.
 23 Why is that? In part that is because there must
 24 be a causal nexus. I want to talk about that nexus
 25 requirement. The purpose of the causal nexus requirement is

1 to show that the patentee is irreparably harmed by the
2 infringement, right; not simply by sales of the product, but
3 specifically by the infringement and by the invention that
4 is embodied in a patent claim.

5 And what the Court explained here, what the
6 Federal Circuit explained here is that sales of an
7 infringing product prove nexus only where the infringing
8 product contains no feature relevant to consumers purchasing
9 decision other than what the patent claims.

10 So what is the record here? The record here is
11 that Jazz urged upon the Court in Motion in Limine No. 1
12 that the patent claim was not directed to once-nightly
13 medicine. Nowhere in the Court's opinion is there any
14 requirement that the modified release particles help a
15 patient stay asleep throughout the night. Jazz explicitly
16 disclaimed that as being part of its invention. And in
17 reliance on Jazz's assertion this court agreed. And in this
18 Court's order on the motions in limine that held that
19 there's no requirement that the asserted patents enabled
20 those unclaimed limitations; and, therefore, there was no
21 requirement that this have a controlled release profile that
22 was suitable for once-a-day dosing, that that is not what
23 the claims were directed to, unlike some of the other method
24 of treatment claims that Jazz elected not to pursue at
25 trial.

1 What does that mean? That means, as a practical
2 matter, the question is why do patients select Lumryz? Do
3 patients select Lumryz because it's packaged in a sachet or
4 do patients select Lumryz because, unlike Jazz, Avadel has
5 been able to formulate a product that allows for once-a-day
6 dosing? And I would suggest the answer to that question
7 unambiguously is that patients pick Lumryz because it allows
8 for once-a-day dosing. That is the reason that patients are
9 selecting it and that is something that Jazz has
10 affirmatively disclaimed as being its invention. Its
11 invention is, in its words, packaging. It is making the
12 administration more convenient. It is including the drug in
13 a sachet.

14 Now, do we do that? Yes, absolutely, we do
15 that, but that -- there -- again, this is Jazz's burden,
16 Jazz has put forward no evidence, no evidence at all, that
17 patients buy Lumryz because it's packaged in a sachet or
18 even because it has a separate acid associated with it as
19 opposed to having an acid that's an integral part of your
20 formulation, or having the thickener being separate as
21 opposed to being an integral part of the formulation. All
22 of the evidence in the case is that patients take Lumryz
23 because it allows them to sleep through the night. It is
24 suitable for once-a-day dosing.

25 Finally, I want to turn to -- sorry, I want to

1 continue to talk about irreparable harm and whether money
2 damages are sufficient.

3 Now, in *Watera* the Court noted that one of the
4 relevant factors was that *Watera* had not licensed
5 competitors to sell tests. And here Jazz has licensed
6 competitors to sell oxybate. The point that I want to make
7 here is that the harms that Jazz is pointing to are harms
8 from the sale of the loss of market share from both Xyrem
9 and Xywav. And in its public filings -- and this is
10 attached to the declaration of Mohan Rao, it's part of
11 Jazz's 8K for 2023, exhibit 4 to Jazz's opening submission.
12 What Jazz said is that these authorized generic versions of
13 high sodium oxybate, these are the ones that Jazz licensed,
14 have negatively impacted and are expected to continue to
15 negatively impact Xyrem and Xywav sales for patients with
16 narcolepsy.

17 So the critical point here, Your Honor, is that
18 in advanced cardiovascular, the Court found that the fact
19 that the patentee was willing to forego its exclusive rights
20 for some manner of compensation shows that money damages are
21 rarely inadequate. That is also true here. Jazz granted
22 nonexclusive licenses to ten different manufacturers of
23 generic Xyrem. Those were patents protecting -- some of
24 them both Xyrem and Xywav. Now, I heard a representation
25 from counsel that they only pertain to Xyrem, but they are

1 listed in the Orange Book for both -- some of them for both
2 Xyrem and Xywav, including U.S. Patent 8,772,6306 and
3 9,050,302. Both of those patents included in the licenses,
4 both of those patents listed in the Orange Book for both
5 Xyrem and Xywav.

6 So the critical point here, Jazz has been
7 willing to license patents that directly cover the very
8 products that are at issue here that they say that they are
9 trying to protect. We are one step further removed from
10 that because we are talking about a patent that doesn't
11 actually cover those products, so it is highly relevant that
12 they willingly licensed for consideration patents that
13 directly cover the products that they say that they are
14 trying to protect. That shows that Jazz has found that
15 money damages, that consideration, is adequate in lieu of
16 simply insisting upon exclusivity.

17 The final point I want to touch on, Your Honor,
18 is repetitional harm. First of all, in the *Baxalta* case,
19 the Court found that repetitional harm was relevant only
20 where a plaintiff itself practices the patented invention,
21 which is not the case here. But, moreover, in that case the
22 Court found most plausible the testimony of witnesses that,
23 if anything, the patent holder's repetition would be harmed
24 not helped by an injunction.

25 The reason the Court in *Baxalta* held that was

1 that the Court found that taking away a differentiated
2 treatment for patients was the thing that would give rise to
3 repetitional harm. Everyone in this industry and in this
4 market knows that Jazz does not have a once-nightly solution
5 for narcolepsy and that Jazz's once-nightly solution for
6 idiopathic hypersomnia cannot help most patients who need a
7 higher dose, and that Avadel is the one who innovated and
8 who was able to bring that product to market. Those are
9 just already known facts on the ground.

10 We have put in evidence that, if anything, the
11 thing that is detrimental to Jazz's repetition as a company
12 that supposedly cares about patients is the fact that it is
13 seeking an injunction against a product that gives rise to a
14 differentiated benefit for patients. That is the thing that
15 is giving rise to repetitional harm.

16 I want to note that Jazz cited a case on this
17 irreparable harm question *EZ Guard* and sort of suggested
18 that the fact of competition alone was sufficient to find
19 that there would be impairment of plaintiff's goodwill and
20 repetition. But the thing that I want to note about that
21 case is the Court found that in the case at issue the
22 defendant had hired away the plaintiff's employees in
23 violation of noncompetes, had engaged in a marketing
24 campaign that the Court characterized, as I think, wrongly
25 placed from the beginning, and there were a number of other

1 reasons that the Court found in that case that the defendant
2 had engaged in conduct that would give rise to repetitional
3 harm.

4 I want to note here that we heard a lot about
5 Avadel's marketing literature. First, as the Court noted in
6 *Abbott*, if they have a problem with the way that we are
7 marketing or selling, they should take steps against the way
8 that we are marketing or selling. They're not doing that
9 because the conduct at issue is industry standard conduct
10 and because everything we have said is true. But if they
11 think it is not that is the remedy, not enjoining sales of
12 the product itself.

13 So with that, the final point that I want to
14 touch on, Your Honor, is the question of unclean hands. So
15 with respect to unclean hands, there is a general maximum
16 that he who comes into equity must come with clean hands.

17 We are not asserting unclean hands as an
18 affirmative defense. Although I will note it is not one of
19 the affirmative defenses that Rule 8 specifies must be pled.
20 Rule 8 lists a number of affirmative defenses must be pled,
21 unclean hands is not one of them. But we are not asserting
22 this as an affirmative offense. We're saying there's a
23 general maximum that when you seek an equitable relief as in
24 an injunction, you must come with clean hands. And this
25 court being called upon to exercise its discretionary

1 equitable power can and should look at all of the relevant
2 considerations.

3 In this case, as the Court knows, Jazz
4 improperly listed its REMS patent in the Orange Book and
5 used that to delay Avadel's approval by a year -- over a
6 year and a half. That was essentially self-help on Jazz's
7 part that resulted in substance and an injunction, because
8 that is what, in effect, that mandatory stay of approval was
9 for over a year and a half. And in evaluating here Jazz's
10 request for a permanent injunction, we think the Court can
11 and should take into account that Jazz got the benefit of
12 over a year and a half of exclusivity that it was not
13 entitled to as a function of its conduct with respect to the
14 REMS patent, and that that is germane to the Court's
15 decision in evaluating the overall equities of the case.

16 THE COURT: All right.

17 MS. DURIE: And that concludes my presentation.
18 I take that back, I have one more slide, thank you. The FTC
19 looked at this conduct, as the Court knows, and the FTC, in
20 its statement regarding Jazz's conduct, said that there is
21 good reason to be concerned about improperly listed patents
22 in the Orange Book; that Avadel developed the formulation
23 that we know about, Lumryz; that after this court ordered
24 delisting, the Federal Circuit court eventually held the
25 patent was improperly listed in the Orange Book and ordered

1 it to be delisted; that following that the FDA granted
2 approval and that in the words of the FDA -- I'm sorry, in
3 the words of the Federal Trade Commission in that
4 intervening period, Jazz continued to rake in monopoly
5 profits and patients were deprived of a potentially superior
6 formulation of a critical narcolepsy drug.

7 The Court can take that into account in making
8 its decision in this case. And I would suggest we have
9 heard FDA talk about the importance of Lumryz, we see FTC
10 talking about this being a credible narcolepsy drug, there
11 is no reason to think that once Avadel does a clinical trial
12 and once Avadel is able to generate that evidence that same
13 statement will not apply to patients with idiopathic
14 hypersomnia too.

15 THE COURT: All right.

16 MR. CERRITO: Your Honor, may I briefly -- we've
17 already been adjudicated with unclean hands without any
18 pleadings, without any facts, without any outcomes of any of
19 the other arguments here. Those statements have nothing to
20 do with the '782 patent. Unclean hands isn't in this case
21 and it's not relevant.

22 You heard counsel testify quite a bit. One
23 might think that she got a medical degree in her little
24 hiatus from the trial. When it comes to people who do have
25 a medical degree, Dr. Bogan, she forgot to mention, I

1 directly took on the issue and said Xywav was effective for
2 once-nightly treatment for IH. And he also went on to say
3 that waking up once a night is not material in IH patients
4 and talks about the adverse events that I had mentioned
5 earlier, so there is testimony from him.
6 What we didn't hear is any reason why they
7 couldn't make a noninfringing alternative. What we heard
8 was well, we spent a lot of money. Okay. Some costs,
9 irrelevant. In both -- I got two case cites for you on
10 that. Sorry. I have to get those cites. *Acumed* and *i4I*.
11 It matter what happens at the time not what happened in the
12 past. So they haven't said they couldn't do it, they
13 clearly can and they've chosen not to.
14 Interestingly enough, on the IH -- it was a very
15 good question Your Honor asked: How could you possibly go
16 bankrupt when you don't have the IH approval now? Because
17 it's nonsense. And if that was true, I would expect the
18 disclosures from this company, public disclosures making
19 that statement in their -- it's nowhere to be found. It's
20 nowhere to be found. They don't say anywhere in their SCC
21 disclosures if we don't get IH approval, we will go
22 bankrupt. Never said that. And if it is true, I guess
23 they'll be making disclosures this afternoon.
24 The fact is that there's noninfringing
25 alternatives, they chose not to do it. It's because --

1 whatever reason they knew before they went into this case,
2 before this trial started, they launched at risk. They had
3 the ability to change, they chose not to, and they chose to
4 do it at risk any way.
5 On the casual nexus, it's a formulation patent,
6 it's not a method-of-use patent.
7 For administrability and stability, it is the
8 formulation that causes that; there would be no product
9 without that formulation. It does not exist without that
10 formulation.
11 It's interesting, counsel complained we didn't
12 have any evidence that somehow it imparted -- I forgot the
13 phrase she used -- certain benefits to patients. Patient
14 number two that counsel put in says there was a benefit to
15 the sachet because she doesn't like carrying the bottles for
16 Xyrem. Sounds like a benefit. Their own patient put in
17 that testimony.
18 THE COURT: Let me ask you a question.
19 MR. CERRITO: Yes, Your Honor.
20 THE COURT: Does generic Xyrem compete with
21 Xywav?
22 MR. CERRITO: No, they are not substitutable.
23 And let's go back to that, there is no license.
24 Just so I'm 100 percent clear -- counsel I think misquoted
25 me. I never said the word "patents" that covered it, I said

1 there is no license to Xywav. We have none. We've given
2 none and we will not give any.
3 THE COURT: So the statement is that Jazz was
4 willing to license patents that cover Xyrem and Xywav, U.S.
5 Patent number 8,772,6306 and 9,050,302, do they cover Xyrem
6 and Xywav?
7 MR. CERRITO: I apologize, I don't know the
8 numbers off the top of my head. We do have patents that
9 cover both products. We only licensed them to settle
10 litigation on Xyrem. We have never licensed them with
11 regard to Xywav.
12 The settlement of litigations -- the *Acumed*?
13 (Discussion held off the record.)
14 *Acumed*, *Sanofi*, *Douglas Dynamics* all talk about
15 settling litigations and licensing patents -- not even the
16 patent-in-suit here, by the way. But doing that and
17 settling litigation should not go against the entry of a
18 permanent injunction. Again, it's not even the patent that
19 we're here talking about.
20 I want to go back for a second -- and we're
21 going to talk about IH for just minute. But the idea that
22 somehow they -- it's an interesting question, and it sort of
23 struck me when she said it that they'd be under safe harbor
24 to perform clinical trials for IH. I don't think that's
25 accurate. She's an adjudicated -- she, sorry. Their

1 company is an adjudicated infringer. I'm not sure they get
2 around -- I don't think they get a safe harbor provision
3 when you're an adjudicated infringer.
4 Having said that, we're not seeking to enjoin
5 the injunction -- the judgment would not go to clinical
6 trials, we don't have a problem -- but I'm not sure they get
7 a free ride for that after having been adjudicated an
8 infringer.
9 Having said that, we heard quite a bit, quite a
10 bit about how great Lumryz is for IH. We don't even know if
11 it's going to get approval. We don't even know at what
12 dosage strengths it would get approval. We don't know what
13 the IH indication would look like; is it going to be
14 different, is it going to be the same? There's a lot of
15 speculation that they would get some kind of superiority.
16 It's all speculation. They have no evidence of it
17 whatsoever. Not a single shred. To say that they would
18 automatically get this superior approval, there's no basis
19 for that.
20 THE COURT: How do you respond to the statements
21 and argument by Avadel pointing out that during the trial
22 Jazz represented that Claim 24 had nothing to do with
23 once-nightly dosing?
24 MR. CERRITO: It has -- it does not because it's
25 not a method-of-use claim, that's correct. But that product

1 doesn't exist and hence give them the ability to sell it for
2 once-nightly without that formulation. It doesn't -- there
3 is no product so they could -- there would be nothing to
4 sell. There would be nothing to be approved. There would
5 be nothing that was stable and administrable without that
6 formulation. And as patient two said she looks the sachet a
7 lot better than the bottles. That's why she likes it.

8 THE COURT: But Avadel doesn't dispute that
9 patients buy Lumryz for once-nightly dosing?

10 MR. CERRITO: That's what -- that is the
11 indication, correct. Not to be -- I don't know why they buy
12 it. I can't get in their head, but that's the indication.

13 THE COURT: All right.

14 MR. CERRITO: The discussion of once-nightly
15 Xywav was centered upon their interpretation of data.
16 Again, I'm not sure there's evidence on this other than
17 attorney argument concerning the amount of patients in a
18 clinical trial that were taking once- or twice-nightly for
19 whatever reason. They make the bold statement sitting here
20 today that the vast majority is for twice-nightly. There's
21 no evidence of that. They have not -- this is what I said
22 in my opening, cited nothing for it, there's no article,
23 nothing that they support their statement.

24 The reality is it's approved for once-nightly --
25 and if you think about it maybe once-nightly and

1 twice-nightly is the better way to do it, giving patients
2 options, not solely one option. And, by the way, they say
3 the dose may be higher, keeping patients asleep longer,
4 that's not their problem, by the way. IH patients sleep a
5 long time, that's not the problem, it's waking up and being
6 refreshed, so maybe the longer dosing or more dosing would
7 be worse for them. These are different disease states.

8 And for counsel to say oh, we would be superior,
9 it would be better for them, there's no evidence for that.

10 This is science. You have to run the studies. You have to
11 do the math, if you will. There's no evidence that any of
12 that is accurate, it's all made up attorney argument.

13 I couldn't say it the other way either, I'm not
14 saying it won't be better, but certainly there's no
15 evidence -- they have to come forward, haven't heard a
16 single thing that would support that.

17 Again, going back for a second of noninfringing
18 alternatives. After all that discussion, timing and some
19 costs, again, which don't matter, you didn't hear them say
20 they don't have one. She did not say that. She never said
21 that. So the ability to make that change or switch into a
22 product to get away from infringing our product exists. She
23 never denied that.

24 Sorry, Your Honor, just one more second. Just
25 want grab it up quickly. The *United Therapeutics* case that

1 they cited to Your Honor at the end of the day, that case
2 was a preliminary injunction case. They found that there
3 was unlikely to find price erosion, lost sales, all those
4 things, it's not particularly relevant to what we're sitting
5 here today talking about.

6 With regard to the data that they showed you
7 from the clinical -- it wasn't clinical trial, from the data
8 about the difference between the once-nightly and
9 twice-nightly Xyrem, I told you they showed you an
10 incomplete document. The complete is here. See the numbers
11 are different. This is the clinical assessment done by the
12 FDA, not a statistician. This is actually what the FDA did.
13 And the paragraph directly before that, if you just scroll
14 up a little bit, begins "similar..." again, here we say:
15 "Similar trends were also observed in subgroups." You drop
16 down to once-nightly versus twice-nightly. So they are
17 showing similar trends between once-nightly and
18 twice-nightly dosing. They didn't show you the whole
19 document.

20 With that, Your Honor, I think we're clear here
21 that we've shown all of the elements here. Despite what you
22 heard, despite what you heard was a lot of nonevidence, a
23 lot of argument from counsel on the other side, the reality
24 is they are an adjudicated infringer. This is a
25 pharmaceutical space. Yes, choice is good, but if you're --

1 if that's the only option, you would never get injunctions
2 in this space. It simply cannot be. We can supply the
3 market, we have products available, certainly in the IH
4 market.

5 Thank you for your time.

6 THE COURT: All right.

7 MS. DURIE: Your Honor, I'd like to just provide
8 two record sets, if I may.

9 The first is with respect to the question of
10 competition from the licensees with Xywav. Jazz's 10-K for
11 2023, it's exhibit 4 to Jazz's opening brief at page 35,
12 says accordingly: "Beginning in January 2023, Xywav and
13 Xyrem face competition from an AG version of sodium
14 oxybate." That's an authorized generic version.

15 The second citation was 271(C), which begins "it
16 shall not be an act of infringement..." that is the section
17 that includes the safe harbor for regulatory submissions to
18 FDA. 271(e) "it shall not be an act of infringement..."
19 and then goes on to say generating data to submit to FDA.

20 THE COURT: All right.

21 MS. DURIE: Thank you.

22 THE COURT: All right. Let's take a break.

23 Let's give the court reporter a break, a 10-minute break.

24 We'll come back and finish up.

25 (Break taken.)

1 THE COURT: All right. You may be seated.
2 Let's talk about the royalty.
3 MR. CALVOSA: Good afternoon, Frank Calvosa from
4 Quinn Emanuel on behalf of plaintiffs, and I'll be
5 presenting on the ongoing royalty today.
6 So Jazz's ongoing royalty request could be
7 broken up into two categories. The first is if an
8 injunction is granted, the ongoing royalty would apply from
9 the time of verdict to all current patients who are on drug
10 up until the time of the effective date of the injunction;
11 remember that's the injunction that we're asking for. If no
12 injunction is granted, then it would be all current and
13 future patients that the ongoing royalty would apply to.
14 And I'll just throw one more out there if some sort of
15 injunction is shaped where it applies to IH but not
16 narcolepsy, the royalty would apply to patients who are
17 carved out of the injunction or not encompassed within the
18 injunction.
19 THE COURT: Okay.
20 MR. CALVOSA: Avadel's own case that they cited
21 in their opposition support that an ongoing royalty is
22 appropriate here. And that is the Northern District of
23 California's *Apple v. Samsung* case and there it cites
24 *Telcordia v. Cisco* from the Federal Circuit in 2010. And it
25 explains the purpose behind the ongoing royalty is to stop

1 serial lawsuits, right, so we don't have to come back here
2 every time Avadel infringes and sue them again.
3 There's basically two scenarios where an ongoing
4 royalty is not applied, neither of which is relevant here.
5 The first is if the parties agree with the Court orders, the
6 parties can negotiate. The parties haven't asked for that
7 here.
8 The second is if the jury's verdict applied not
9 only to past damages, but also was a paid up lump-sum or
10 applied to an ongoing royalty as well. Here it's very clear
11 from the jury's verdict form and from the jury instructions
12 the jury's verdict was for past infringement for the past
13 sales. There was no paid up lump-sum like Avadel argues
14 maybe happened in their opposition.
15 So let's get to the ongoing royalty request from
16 Jazz, and that is from March 4, 2024, the time of verdict
17 through the year 2025, 27 percent. From 2026-2032,
18 13 percent. And 2033 through the expiration of the patent
19 in 2036, 3.5 percent. If this looks familiar, the Court and
20 I'm sure Avadel will point it out, this was based on
21 Dr. Rainey's testimony at trial and it remains rebutted.
22 Avadel did not bring any damages witness to
23 trial. Although Avadel submitted a declaration from Mohan
24 Rao on certain economic issues with the injunction brief,
25 Dr. Rao did not say that this was an inappropriate or

1 ongoing royalty. And we had no testimony whether at trial
2 or in the declaration from Mr. Divis that Avadel would not
3 be willing to pay this royalty.
4 And we had testimony at trial from Jazz's
5 corporate representatives that Jazz didn't even want to
6 license the patent at all. So, again, Dr. Rainey's
7 testimony is un rebutted and Jazz respectfully submits -- and
8 we'll deal with post-trial briefing that the jury's verdict
9 of the 3.5 percent for the entire time was unsupported.
10 Now, I'm going to move on to slide 78 for Your
11 Honor, but to avoid sealing the courtroom I'm just going to
12 direct to certain portions, but not publish it on the
13 screen.
14 THE COURT: All right.
15 MR. CALVOSA: Now, Dr. Rainey's un rebutted
16 testimony was that the '782 patent does not expire until
17 2036 and that a 3.5 percent royalty rate for the entire time
18 would be wholly insufficient to compensate Jazz. And if you
19 look at the *Creative Internet* case out of the Eastern
20 district of Texas it asks for the ongoing royalty: What
21 amount of money would reasonably compensate a patentee for
22 giving up his right to exclude yet allow an ongoing willful
23 infringer to make a reasonable profit? And that's what
24 Jazz's ongoing royalty does.
25 And as Dr. Rainey testified at trial and based

1 on both parties' projections, I won't say the number, but on
2 slide 78 there is the amount of money Jazz projected it
3 would loss should the royalty rate be 3.5 percent the entire
4 time. On the other hand, Avadel said it expects to make
5 over \$6.2 billion, with a B, billion in revenue even after
6 it paid Jazz's ongoing royalty rates. \$6.2 billion after
7 that. So they undoubtedly would make more than a reasonable
8 profit and Jazz would be adequately compensated.
9 Dr. Rainey also testified based on the facts
10 presented at trial that it would be economically irrational
11 for Jazz to enter into a license where they got 3.5 percent
12 for the entire life of the patent.
13 So, the jury, like I said, decided on the
14 3.5 percent, but the only thing we heard as a reason why was
15 Avadel's counsel -- again, no witness from Avadel. Avadel's
16 counsel at trial in closing statements saying that
17 "27 percent would be outrageous." That's a quote. But
18 27 percent wouldn't be outrageous, we saw Avadel would make
19 \$6.2 billion after that and the other staggered royalty.
20 We've seen Courts, including the District of New
21 Jersey here in *Joyal Products* approve a royalty near the
22 profit margin for the infringer. We're not even approaching
23 Avadel's profit margins.
24 And the Federal Circuit has done the same. In
25 the *Arctic Cat* case, which was the Federal Circuit in 2017,

1 the Court affirmed an ongoing royalty set at the infringer's
2 profit margin. And it specifically stated that the Federal
3 Circuit has affirmed rates at or near the infringer's
4 alleged profit margin and provides a string cite of cases
5 there. And, again, we wouldn't be approaching that number
6 for Avadel.

7 We also heard Avadel's counsel in trial at
8 closing suggest, as they do in opposition, that Claim 24 is
9 limited to the sachet. You heard earlier today from
10 Mr. Cerrito's presentation -- if we could go to slide 80 --
11 that Avadel's counsel admitted in opening statements that
12 Claim 24 covers Lumryz as a whole. Remember she said it was
13 Avadel's invention; the jury disagreed with that.

14 Jazz's technical expert confirmed through his
15 analysis that Claim 24 covered Lumryz as a whole, and that's
16 what Dr. Rainey relied upon in his opinion.

17 We go back to that *AstraZeneca* case now in the
18 damages context. This case does not fit the multi-component
19 cell phone case facts, right, it's a full formulation that
20 covers the infringing product. You can't slice and dice it
21 up and say oh, we can attribute this valve or that valve.
22 Here there would be no sale of Lumryz but for the stability
23 of the product and its administrability.

24 Now, on from the royalty rate to the royalty
25 base. There was a suggestion in Avadel's opposition that

1 is the actual gross sales which, again, the gross sales
2 number nobody even said that should be the royalty base,
3 everybody agreed it should be net sells, and that was that
4 \$32 million number we saw. But if you go going to use gross
5 sales through January 1, 2024, the actual correct number
6 would be much higher, it would be 48, even higher than Jazz
7 asked for as a royalty base in January.

8 So, again, Jazz respectfully submits that the
9 jury got the verdict wrong, but even so, putting that aside,
10 this court has the discretion and should award a higher
11 ongoing royalty rate than that that the jury awarded
12 pre-verdict based on that hypothetical negotiation. And we
13 have cases here from the Federal Circuit and this District
14 that explain the reason behind awarding a higher ongoing
15 royalty rate. And in the *Amado*, Federal Circuit case from
16 2008, the Federal Circuit explains that prior to judgment
17 the liability for infringement, the validity of the patent
18 is uncertain, but it's a different calculus once judgment
19 has entered.

20 The *Telcordia*, who was Judge Sleet, discussed
21 how an ongoing royalty rate at a higher rate is appropriate
22 because otherwise a defendant has the incentive to litigate
23 it fully through to the bitter end because there's no
24 downside in losing. There's no change to legal status,
25 which is inconsistent with what the Federal Circuit said

1 the jury apportioned to royalty base by a factor of 5, so it
2 was about 20 percent of what Jazz asked for. And they --
3 Avadel comes up with that based on the royalty base the jury
4 use of that \$6,673,000 figure on top over the \$32,519,000
5 figure on the bottom of that first equation up there. And
6 that was Avadel's gross sales through September 6, 2023 over
7 the net sales number that Dr. Rainey used through
8 January 31, 2024. If you do that calculation, it's not
9 20 percent. Nor did the jury divide by five, you would have
10 gotten a whole number if you would have done that; you don't
11 get the very specific number that the jury used.

12 And if you remember the jury asked a question
13 about the royalty base because Dr. Rainey's number was not
14 in any document. He had done calculations and presented
15 verbally at trial. And what we submit the jury did -- and
16 if you go to the next slide -- is the jury found a number
17 down to the exact penny the same that was in Avadel's weekly
18 sales report from September 6, 2023. The jury made a
19 mistake. There's no doubt that it wasn't this divided by 5
20 or 20 percent. You don't get the numbers when you do that.
21 Where you do find that number down to the exact penny is in
22 Avadel's September 6, 2023 sales. So there was no basis to
23 apportion the royalty base and the jury did not apportion
24 the royalty base.

25 If we go to the next slide what you'll see here

1 actually happens in *Amado*. And Judge Sleet in that
2 *Telcordia* case did award a higher ongoing royalty rate.

3 Judge Stark has also done the same thing in the
4 *DuPont* case that we attached as exhibit 19 to our opening
5 brief.

6 And the *Creative Internet* case out of Eastern
7 District of Texas 2009 explains it really well, and it says
8 because of the hypothetical negotiation, the alleged
9 infringer is just that, an alleged infringer who is a
10 willing licensee. But once that verdict comes down, the
11 alleged infringer, who is a willing licensee, becomes an
12 adjudicated infringer, who is now in a position where they
13 have to take the license.

14 Now, Avadel will probably argue that you
15 shouldn't award the higher ongoing royalty rate because,
16 again, the jury rejected what we asked for. But in *Active*
17 *Video Networks v. Verizon*, that's Federal Circuit 2012, the
18 Federal Circuit affirmed a higher royalty rate even though
19 there was testimony from the defendant, which doesn't exist
20 here, that they would not have agreed to that royalty rate;
21 and even though the jury rejected that royalty rate, the
22 Federal Circuit affirmed the higher rate solely because of
23 the jury's verdict and the changed legal status that the
24 defendant was now an adjudicated infringer. And that's at
25 1342-43 of the *Active Video* case.

1 I'm on slide 86 here. You'll see several
2 examples, including from the Federal Circuit in this
3 District of awarding higher ongoing royalty rates. That is
4 the common practice. I know we have the *Purwick* case where
5 that wasn't done, but the common practice and what the
6 Federal Circuit instructs is that you must consider, the
7 Court must consider the changed legal position post-verdict.

8 And here there's several factors that go into it
9 -- I'll just note a couple of cases up here for the Court.
10 But the *Boston Scientific v. Cordis Corp* case from this
11 district in 2012, that was Judge Robinson saw the royalty
12 increase from 2.95 percent to 32 percent in a line of cases
13 where an injunction had been denied before based on the
14 public interest factor. So the royalty rate was increased
15 to 2.95 percent to 32 percent to allow for that infringing
16 conduct to go forward and to adequately compensate the
17 patentee.

18 Similarly in the *Telcordia* case we talked about,
19 the defendant made a decision to not introduce a
20 noninfringing alternative going forward and to willfully
21 infringe continuing in the future, just like the decision
22 Avadel is making now. I heard Avadel's counsel mention
23 about the fact that in the jury trial there was a
24 stipulation that there was no noninfringing alternative.
25 That is different in terms of both the injunction and the

1 District explaining that the culpability for willfulness is
2 measured at the time of the challenged conduct.
3 Second, I mentioned that the uncertainty
4 regarding Claim 24 is gone. Here we have Avadel's counsel
5 cross-examining Dr. Rainey and introducing that uncertainty
6 and questioning the validity that came -- that was supposed
7 to be assumed or presumed based on the ongoing damages case
8 law at the type of the hypothetical negotiation. And she
9 says to him, you know, although patents are presumed valid,
10 the validity of many patents is challenged in court. He
11 said of course he knows that happens and not all patents
12 challenged in court survive. That's true. Some get
13 invalidated, that's true.

14 So Avadel introduced the uncertainty of Claim 24
15 to the jury.

16 And, lastly, as I mentioned, Avadel has not
17 taken any step since it has been found to be an infringer to
18 introduce any of the noninfringing alternatives it claims to
19 have in its patent and has told the world that it has. And
20 courts, including in this District -- and we have a couple
21 of examples here *Telcordia* and *Syntrix Biosystems* cases have
22 increased the royalty rate based on that factual pattern and
23 the other factual patent that we saw.

24 And the last thing I'll mention is that we have
25 a lot of talk today how Claim 24 doesn't add anything. The

1 ongoing royalty.

2 The noninfringing alternative in terms of
3 damages under 283 is measured at the time of the
4 hypothetical negotiation, so could they have gotten it up
5 and running and did they want to get it up and running as of
6 June of 2023. And Avadel said in an interrogatory response:
7 We have no noninfringing alternative. So that was the
8 evidence presented at trial. The question for ongoing
9 royalty and injunction as well, not to double dip into both,
10 but is today do they have an noninfringing alternative or
11 could they introduce one in the future.

12 So talking about the change legal positions,
13 there's three of them and we'll go through them one-by-one,
14 but first is Avadel is now a willful infringer. The jury's
15 verdict extinguished any uncertainty regarding Claim 24's
16 validity. And Avadel has not taken any steps to introduce
17 any possible noninfringing alternative.

18 There is no doubt that Avadel is now a willful
19 infringer. Again, taking the reasoning from *Telcordia* if we
20 were to come back in serial suits, sue them again today
21 instead of getting an ongoing royalty, they would be an
22 adjudicated willful infringer. It's measured at the time of
23 the culpable conduct, starting at the time of that jury
24 verdict valid and infringed they became a willful infringer.
25 And here we have the *Boston Scientific* case from this

1 Apple v. Samsung case, that 2014 one from the Northern
2 District of California at star 16, talks about how an
3 argument like that -- how the invention is invaluable is
4 really rebutted in the fact that the defendant is choosing
5 to continue practicing the invention. And in that court,
6 the *Apple* court found that that was reason to increase the
7 royalty rate going forward.

8 THE COURT: All right.

9 MR. CALVOSA: Any questions, Your Honor?

10 THE COURT: Give me the cite for the *Apple v.*
11 *Samsung*.

12 MR. CERRITO: That's 2014 Westlaw 6687122 and
13 that's at star 16, and I believe it continues a little bit
14 into star 17. And that Northern District of California.
15 November 25, 2014, it's Judge Cohen's opinion.

16 THE COURT: All right.

17 MR. CALVOSA: Thank you, Your Honor.

18 MS. DURIE: Thank you, Your Honor.

19 The first premise of the task before the Court
20 is to determine the appropriate compensation for ongoing
21 infringement in view of the jury verdict. And I want to
22 note that we heard a lot of statements from Jazz's counsel
23 about unfeathered infringement and things of this nature.
24 But in the event that the Court concludes that an injunction
25 is not appropriate, Jazz does receive compensation in the

1 form of a reasonable royalty for the future infringement;
2 and that compensation is predicated upon the jury's
3 determination with respect to what is a reasonable royalty.
4 Here the jury made a determination that a royalty rate of
5 3.5 percent is appropriate.

6 Now, Jazz has not provided any new evidence, any
7 new argument to this court with respect to changed
8 circumstances in terms of facts on the ground, about the
9 market, about competition, about sales, about new license
10 agreements that would justify a departure from what the jury
11 determined. Sometimes that happens. Sometimes parties come
12 in and they present a new analysis in support of a different
13 number, but Jazz didn't do that here. All Jazz did was
14 recapitulate Dr. Rainey's analysis, which the jury
15 considered and which the jury concluded resulted in a
16 royalty rate of 3.5 percent. And so crediting the jury's
17 analysis that is the appropriate royalty rate for the Court
18 to adopt.

19 Now, it is true that in some cases courts have
20 found that it is appropriate to bump up the rate from what
21 the jury found for various reasons. I do want to note,
22 however, that Avadel has not been found to be a willful
23 infringer. In one of the cases that Jazz relies on, the
24 *Joyal* case, that was the 26 percent rate, the defendant had
25 stipulated in the course of trial to being a willful

1 infringe a valid claim, and that is exactly the same
2 construct as the hypothetical negotiation. And that's why
3 in *Purwick* Judge Norieka said it doesn't make sense to
4 increase the amount that the jury found because the jury was
5 analyzing exactly the same situation; you assume
6 infringement, you assume validity, what is an appropriate
7 royalty rate.

8 And indeed in this case, Your Honor clearly
9 instructed the jury that in considering the hypothetical
10 negotiation, you must assume that both parties believed the
11 patent to be valid and infringed. That was the jury
12 instruction and there is no basis for believing that the
13 jury disregarded the Court's instruction in arriving at a
14 royalty rate.

15 Now, Jazz's argument is that we somehow mislead
16 the jury during Dr. Rainey's cross-examination into
17 disregarding the Court's instruction. And they argued in
18 their brief, as we just heard, that we suggested that the
19 uncertain validity of Claim 24 should factor into the jury's
20 damages analysis. That is not what we did. This is the
21 entirety of this portion of the cross-examination of
22 Dr. Rainey to which Jazz cites. This is a very standard
23 opening to the cross-examination of a damages expert. It is
24 designed to make clear to the jury that the testimony of the
25 damages expert is only relevant if the patent is found to be

1 infringer. The Court looked at a litany of litigation
2 misconduct that it found justified in that case an
3 enhancement of the amount of damages to account for that.

4 Jazz could have asked the jury to find that
5 Avadel was willful, it did not. And when the Court's
6 analyzed this question, they looked separately at the
7 question of what was the rate, including whether there
8 should be any departure from the jury verdict in setting a
9 rate, and then whether there should be any enhancement for
10 purposes of willful infringement, which is not at issue here
11 because there has been no willfulness determination.

12 Now, with respect to when an adjustment to the
13 rate that the jury found is appropriate, Judge Norieka
14 addressed that question in the *Purwick* case. And in that
15 case she said that she was not persuaded that the plaintiffs
16 had pointed to any factors to indicate that it would be
17 entitled to a higher royalty rate than the rate determined
18 by the jury.

19 Now, in that case she did go through and
20 identify some circumstances in which a higher rate might be
21 appropriate. For example, if there were new license
22 agreements or if the competitive situation was different
23 from the evidence that had been presented to the jury. But
24 Jazz has made no such argument here. The only argument that
25 Jazz has made here is that Avadel has now been determined to

1 valid and infringed; and that is exactly what Ms. Davis Did.
2 She asked: You're making certain assumptions,
3 you don't have any opinions about infringement, you also
4 don't have any opinions about validity?

5 Right. I just assumed the patents are valid and
6 infringe, but I don't have any opinions on that.

7 The validity of many patent is challenged in
8 court, not all the patents that survive -- that are
9 challenged survive, some patents get invalidated. If Avadel
10 wins in this case, there are no damages.

11 And he said, you know, I'm not a lawyer, my
12 understanding is if validity and infringement are proved
13 then there wouldn't be damages, but hey I'm not a lawyer.

14 That was the point of that line of questioning,
15 it was not to try to negate the jury's instructions, which
16 both sides agreed to because they were correct.

17 Now, the jury was also instructed, Your Honor,
18 that the total royalty rate should reflect the value
19 attributable to the infringing features of the product and
20 no more. And that it should distinguish that from
21 nonpatented features, the manufacturing process, business
22 risks or significant features or improvements added by
23 Avadel. There was extensive testimony at trial about
24 Avadel's contributions, about the fact that Avadel was the
25 one who figured out how to make a once-nightly formulation

1 of oxybate. And under the Court's instructions, the jury
2 absolutely appropriately could take that evidence into
3 consideration in making its determination as a matter of
4 fact applying these instructions about what Jazz had
5 contributed and what Avadel had contributed. What would be
6 a fair and reasonable royalty rate for the use of the
7 increment that Jazz had contributed, and that is exactly
8 what the jury did.

9 Now there has been some discussion about the
10 amount of past sales that the jury wrote down following the
11 jury's determination as to a reasonable royalty. As the
12 Court will recall, this was the subject of a question that
13 was posed by the jury during jury deliberations. And it was
14 also the subject of an answer that the Court gave to that
15 question to the jury before the jury rendered its verdict.

16 This was the Court's answer agreed upon by both
17 sides, so Jazz agreed to this. Dr. Rainey testified that
18 the amount of net sales is \$32 million and change. Avadel
19 did not present a damages expert that contested that number,
20 but, critically, it is up to the jury to decide whether to
21 believe Dr. Rainey and how much weight to give to his expert
22 testimony.

23 Both sides agreed that was the appropriate
24 instruction, that was the instruction that was given, the
25 jury then rendered its verdict.

1 In our view, Your Honor, there is no reason for
2 this Court to depart from the jury's determination, which we
3 think is binding, absent post-trial proceeding, but as we
4 sit here today it is binding that 3.5 percent is a royalty
5 rate. And as was the case in Judge Norieka's decision there
6 has been no reason that has been given for changed
7 circumstance that would warrant departing from that, because
8 then, as now, the operative assumption is that Avadel needs
9 a license because it is infringing a valid claim.

10 I would note that in the *Apple v. Samsung* case
11 that Jazz cited, Jazz had said at trial to the jury the
12 design-arounds would be simple or already exist, and that
13 there was a difference there with respect to lock-up that
14 reflected the Judge's different view of what would
15 constitute a reasonable royalty in that case. Here Jazz has
16 chosen to present no evidence to the Court above and beyond
17 a recapitulation by Dr. Rainey that says I still think I was
18 right, but the jury evaluated and as to which the jury
19 rendered a verdict.

20 So our request, Your Honor, would be that this
21 court give affect to the jury's verdict. And as we said in
22 our papers, I think there is more than one way to interpret
23 what the jury did with respect to the base. I think it is
24 plausible that in view of this instruction that it was up to
25 the jury to decide how much weight to give to his testimony

1 and what to do that they, in substance, apportioned the
2 base. But at worst, from Avadel's point of view, the "jury"
3 should adopt the 3.5 percent reasonable rate that the jury
4 found sufficient to credit Jazz for its contributions while
5 also recognizing Avadel's contributions and award that as a
6 reasonable royalty going forward.

7 Thank you.

8 MR. CALVOSA: Just very briefly, Your Honor.
9 Just addressing the first comment that Ms. Durie made about
10 there's no new circumstances here and she gave a list of
11 different points of evidence that could be introduced as new
12 circumstances. Several of those overlap with the discovery
13 that Jazz requested and that Avadel opposed post-trial,
14 where you have to look how to change post the jury verdict.
15 Jazz requested that discovery, Avadel opposed and the Court
16 sided with Avadel and denied Jazz's discovery request. So
17 Jazz did not have an opportunity to take new discovery on
18 the changed circumstances post-verdict, which only can be
19 taken post-verdict. Dr. Rainey took that into account in
20 his declaration and given that he went to the royalty rate
21 that he provided. And I cited you that *Active Video* case
22 from the Federal Circuit, which Avadel does not address, has
23 never addressed. And in that case there was no willful
24 infringement, the jury verdict alone rejected what the
25 expert originally presented, was not controlling. The Court

1 still affirmed a higher ongoing royalty rate. And that's
2 because *Amado* explains that jury verdict alone is enough.
3 Similar in the *Hynix v. Rambus* out of the Northern District
4 of California that we heard counsel talk about that lock-in.
5 There was no willful infringement, the Court ordered the
6 parties to negotiate an ongoing royalty, specifically noting
7 the *Amado* case and how the higher royalty rate based on the
8 jury verdict alone should be taken into account. And we've
9 cited several examples of that in our briefing.

10 Another thing that counsel mentioned is that
11 they weren't a willful infringer at trial and that we didn't
12 seek enhanced damages. Enhanced damages is under 284 of the
13 code, ongoing royalty under 283. They are two different
14 inquiries. You can get more money through enhanced damages,
15 you could also get a higher royalty through an ongoing
16 royalty. Like I said, courts have routinely implied that,
17 including Judge Stark and Judge Sleet in this District. The
18 Court says you must take that into account, the Court must
19 do that. *Purwick*, respectfully, is an outlier amongst those
20 decisions.

21 The last point I just want to make is in the
22 cases where counsel noted *Apple*, for example, there was
23 testimony that a design-around would be easy. In this case,
24 there's no testimony, there is no evidence, despite the
25 multiple trial witnesses, despite the multiple declarations

1 that Avadel at this point cannot use their noninfringing
2 alternative.
3 Counsel mentioned regulatory lock-in, there's no
4 evidence of that. The lock-in case that she referred to,
5 *Hynix*, specifically states that the testimony regarding the
6 lock-in from both the fact witnesses and the experts that
7 was persuasive, and that's what carried the day here. Here
8 there's no evidence whatsoever, whether through trial
9 testimony or untested declarations that Avadel chose to put
10 in its injunction briefing.

11 Unless Your Honor has any questions, that's all
12 I have.

13 THE COURT: All right. I have no questions.

14 MR. CALVOSA: Thank you, Your Honor.

15 THE COURT: All right.

16 MS. DURIE: May I talk about a housekeeping
17 matter, Your Honor?

18 THE COURT: Yes.

19 MS. DURIE: So I think in the schedule we have a
20 date for providing proposed finding of fact and conclusions
21 of law, which I think pertains to this proceeding. And I
22 think a question in our mind, given the interrelationship
23 between these issues and the JMOL briefing, for which a
24 schedule is yet to be set, I think, does it make sense for
25 us to supply those proposed findings of fact and conclusions

1 filing post-trial motion on the royalty issue, and one of
2 the things that I will consider is whether I just defer
3 decision on that until we deal with --

4 MS. DURIE: Right. We'll be filing post-trial
5 motions on the validity issue.

6 THE COURT: Okay. All right. So I might -- so
7 if I'm hearing you right, Ms. Durie, are you suggesting that
8 the Court defer ruling on this until we deal with the
9 post-trial motion and do it all at the same time?

10 MS. DURIE: I am, Your Honor. For two reasons,
11 obviously on the injunction case it becomes moot if the
12 Court grants a post-trial motion on validity. On the -- the
13 damages point becomes moot, too; in other words, if the
14 Court grants our motion post-trial and reverses the jury
15 verdict on validity, this entire proceeding becomes moot.

16 And on damages, part of Jazz's argument was
17 predicated -- it referenced the fact that it would be
18 seeking to move with respect to the 3.5 percent royalty
19 rate. So from our point of view it makes sense to defer all
20 of this in terms of a ruling until after the Court has ruled
21 on JMOL.

22 THE COURT: All right. Let me hear from Jazz.

23 MR. TIGAN: Your Honor, there was some confusion
24 about the supplemental schedule you entered in March.
25 Paragraph 3 pertains to the injunction briefing, which is

1 in law regarding the injunction and the ongoing royalty now
2 or should we wait until the Court has had an opportunity to
3 review the JMOL papers and then resolve all of those issues
4 together?

5 MR. CALVOSA: May I just add one thing, Your
6 Honor -- and I think we're in agreement on this as well.
7 Given that there was no live testimony at the injunction
8 hearing and given that the parties have already submitted
9 briefs with case law and all the supporting evidence, I
10 think we could skip the findings of fact and conclusions of
11 law related to the injunction and just deal with the JMOL
12 briefing, which I think is consistent with what Ms. Durie
13 proposes.

14 MS. DURIE: I actually thought that -- it wasn't
15 a schedule, I thought the Court actually did want proposed
16 findings of fact and conclusions of law with respect to this
17 proceeding. We're happy to provide them.

18 THE COURT: I didn't -- I think that normally
19 deals with when there's a separate matter for equitable
20 matters that the Court has to decide. I don't recall the --
21 I'll have to go back and look at my order, but given that
22 you know there's no testimony here, I don't need proposed
23 findings of fact and conclusions of law with respect to, you
24 know, this preliminary injunction hearing.

25 I know that Jazz has indicated that it will be

1 done, you've considered it. Paragraph 5 deals with the
2 Rule 50 and Rule 59 motions, which we've been talking about.
3 And in between there was this paragraph about findings of
4 fact and conclusions of law. At least on the Jazz side we
5 were a little confused and had some internal debate about
6 which set of briefing that pertained to. And just at a most
7 basic level, we wanted to get clarity on what you need; do
8 you need it in connection with this hearing and at what time
9 or not at all and we simply brief 50 and 59 motions after
10 judgment, which is what you've set up?

11 THE COURT: All right. I don't need proposed
12 findings of fact and conclusions of law with respect to the
13 preliminary injunction hearing, so that doesn't apply to the
14 preliminary injunction hearing.

15 The question on -- so what's your position on
16 whether the Court should handle this motion and post-trial
17 motions at the same time?

18 MR. TIGAN: Our position, unless my colleagues
19 correct me, is if -- would have the Court decide today's
20 motions, enter judgment. Your order already provides for
21 this 28 days after entry of judgment, it triggers -- under
22 the rules, Rule 50 and 59 motions you have page limits, it's
23 already set up.

24 THE COURT: Okay.

25 All right. I understand the parties' positions

1 with respect to whether or not an injunction, a permanent
2 injunction is granted. The Court is going to decide the
3 issue. I'm going to -- with respect to the ongoing royalty,
4 that may be something that I defer until I get the
5 post-trial motions because even Jazz says that, you know, it
6 plans to file. I'm not saying that's what I'm going to do,
7 but I'm going to think about that more. But I will rule on
8 whether a permanent injunction should be granted or not, but
9 I don't need a proposed findings of fact and conclusions of
10 law.

11 MR. TIGAN: That's helpful, Your Honor. Those
12 were due next week so that's good to know.

13 MR. CERRITO: Thank you, Your Honor.

14 THE COURT: All right. Well, thank both sides
15 for your presentations. The Court will take the matter
16 under advisement and issue a ruling.

17 Now there was -- I think Jazz had made a request
18 to hear some additional motions on the antitrust and trade
19 secret --

20 MR. CERRITO: We did, Your Honor.

21 THE COURT: But I denied that.

22 MR. CERRITO: You did. Yeah, you're just
23 reminding us of the denial, Your Honor.

24 (Laughter.)

25 THE COURT: No. But once I rule on the

1 permanent injunction, I might look at it again to see
2 whether it's something a hearing to be scheduled or argument
3 on that, whether it makes sense or not. I don't have it in
4 my head to understand whether -- you know, what the sort of
5 connections are at this time, but it did occur to me that I
6 might look at that after dealing with these issues.

7 MR. CERRITO: Understood, Your Honor.

8 THE COURT: All right.

9 (Whereupon, the following proceeding concluded
10 at 12:47 p.m.)

11 I hereby certify the foregoing is a true
12 and accurate transcript from my stenographic notes in the
13 proceeding.

14 /s/ Michele L. Rolfe, RPR, CRR

U.S. District Court

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EXHIBIT 8



Avadel Pharmaceuticals Announces First Patient Dosed in Phase 3 REVITALYZ™ Trial of LUMRYZ™ (sodium oxybate) Extended-Release Oral Suspension for the Treatment of Idiopathic Hypersomnia

July 31, 2024 at 4:05 PM EDT

DUBLIN, July 31, 2024 (GLOBE NEWSWIRE) -- Avadel Pharmaceuticals plc (Nasdaq: AVDL), a biopharmaceutical company focused on transforming medicines to transform lives, announced today that the first patient has been dosed in REVITALYZ, a Phase 3 study evaluating LUMRYZ as a potential treatment for idiopathic hypersomnia (IH).

"IH is a debilitating sleep disorder characterized by profound sleep inertia, or difficulty waking up and persistent profound daytime sleepiness. Awareness and diagnosis of IH has increased markedly over the last several years. However, IH patients are severely limited in effective treatment options, representing a large unmet need," said Richard K. Bogan, MD, FCCP, FAASM, Principal of Bogan Sleep Consultants, LLC, and Associate Clinical Professor at University of South Carolina School of Medicine. "The potential of LUMRYZ to treat IH with only a single bedtime dose of extended-release sodium oxybate is promising, and the initiation of the Phase 3 REVITALYZ study marks a significant step toward improving care for those living with IH."

REVITALYZ is a double-blind, placebo-controlled, randomized withdrawal, multicenter Phase 3 study designed to evaluate the efficacy and safety of LUMRYZ given as a once-at-bedtime dose, in IH. The study will enroll approximately 150 adults who are diagnosed with IH and includes an open label extension portion. REVITALYZ enrollment is open for both participants switching from immediate-release oxybates and not currently taking oxybates.

The primary objective of REVITALYZ is to demonstrate reduction in daytime sleepiness as measured by the primary endpoint, change in total score of the Epworth Sleepiness Scale (ESS) at Week 14. Secondary endpoints will evaluate the effect of LUMRYZ on additional efficacy parameters including patient and clinician impression of change, idiopathic hypersomnia severity, and a measure of the functional outcomes of sleep.

"Dosing the first patient in REVITALYZ is an important milestone for the IH community, which has been vocal in the need for more treatment options, particularly an extended-release form of oxybate that would ideally provide full nocturnal drug exposure in a single, once-at-bedtime dose," stated Jennifer Gudeman, PharmD, Senior Vice President, Medical and Clinical Affairs of Avadel Pharmaceuticals. "We are committed to advancing this study and are emboldened by the excitement of experienced clinical trial sites' participation, which reflects the critical unmet need in the current therapeutic landscape."

Additional information about the trial can be found at: <https://clinicaltrials.gov> (ClinicalTrials.gov Identifier: NCT06525077).

About LUMRYZ™ (sodium oxybate) for extended-release oral suspension

LUMRYZ is an extended-release sodium oxybate medication approved by the FDA on May 1, 2023, as the first and only once-at-bedtime treatment for cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy.

The FDA approval of LUMRYZ was supported by results from REST-ON, a randomized, double-blind, placebo-controlled, pivotal Phase 3 trial in adults with narcolepsy. LUMRYZ demonstrated statistically significant and clinically meaningful improvements in the three co-primary endpoints: EDS, clinicians' overall assessment of patients' functioning (CGI-I), and cataplexy attacks, for all three evaluated doses when compared to placebo.

With its approval, the FDA also granted seven years of Orphan Drug Exclusivity to LUMRYZ for the treatment of cataplexy or EDS in adults with narcolepsy due to a finding of clinical superiority of LUMRYZ relative to currently available oxybate treatments. In particular, the FDA found that LUMRYZ makes a major contribution to patient care over currently available, twice-nightly oxybate products by providing a once-nightly dosing regimen that avoids nocturnal arousal to take a second dose.

About Idiopathic Hypersomnia

Idiopathic hypersomnia (IH) is a rare sleep disorder characterized by excessive daytime sleepiness (EDS) not attributable to any other medical conditions or symptom of another medical condition. Symptoms may include prolonged nocturnal sleep of good quality, difficulty in waking up, and brain fog. Additional symptoms may include falling asleep unintentionally, challenges in maintaining focus, and occasional memory lapses. IH can have a significant impact on a patient's quality of life. According to claims data, there are an estimated 37,000 diagnosed IH patients in the United States, although the total patient population may be greater due to some patients who have not yet been diagnosed, have been misdiagnosed, or are not currently seeking treatment.

About Avadel Pharmaceuticals plc

Avadel Pharmaceuticals plc (Nasdaq: AVDL) is a biopharmaceutical company focused on transforming medicines to transform lives. Our approach includes applying innovative solutions to the development of medications that address the challenges patients face with current treatment options. Avadel's commercial product, LUMRYZ, was approved by the U.S. Food & Drug Administration (FDA) as the first and only once-at-bedtime oxybate for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy. For more information, please visit www.avadel.com.

IMPORTANT SAFETY INFORMATION

WARNING: Taking LUMRYZ™ (sodium oxybate) with other central nervous system (CNS) depressants, such as medicines used to make you fall asleep, including opioid analgesics, benzodiazepines, sedating antidepressants, antipsychotics, sedating anti-epileptic medicines, general anesthetics, muscle relaxants, alcohol or street drugs, may cause serious medical problems, including trouble breathing (respiratory depression), low blood pressure (hypotension), changes in alertness (drowsiness), fainting (syncope) and death.

The active ingredient of LUMRYZ (sodium oxybate) is a form of gamma hydroxybutyrate (GHB), a controlled substance. Abuse or misuse of illegal GHB alone or with other CNS depressants (drugs that cause changes in alertness or consciousness) have caused serious side effects. These effects include seizures, trouble breathing (respiratory depression), changes in alertness (drowsiness), coma and death. Call your doctor right away if you have any of these serious side effects.

Because of these risks, LUMRYZ is available only by prescription and filled through certified pharmacies in the LUMRYZ REMS. You must be enrolled in the LUMRYZ REMS to receive LUMRYZ. Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

INDICATIONS

LUMRYZ (sodium oxybate) for extended-release oral suspension is a prescription medicine used to treat the following symptoms in adults with narcolepsy:

- sudden onset of weak or paralyzed muscles (cataplexy)
- excessive daytime sleepiness (EDS)

It is not known if LUMRYZ is safe and effective in people less than 18 years of age.

Do not take LUMRYZ if you take other sleep medicines or sedatives (medicines that cause sleepiness), drink alcohol or have a rare problem called succinic semialdehyde dehydrogenase deficiency.

Keep LUMRYZ in a safe place to prevent abuse and misuse. Selling or giving away LUMRYZ may harm others and is against the law. Tell your doctor if you have ever abused or been dependent on alcohol, prescription medicines or street drugs.

Anyone who takes LUMRYZ should not do anything that requires them to be fully awake or is dangerous, including driving a car, using heavy machinery or flying an airplane, for at least six (6) hours after taking LUMRYZ. Those activities should not be done until you know how LUMRYZ affects you.

Falling asleep quickly, including while standing or while getting up from the bed, has led to falls with injuries that have required some people to be hospitalized.

LUMRYZ can cause serious side effects, including the following:

- **Breathing problems, including** slower breathing, trouble breathing and/or short periods of not breathing while sleeping (e.g., sleep apnea). People who already have breathing or lung problems have a higher chance of having breathing problems when they take LUMRYZ.
- **Mental health problems**, including confusion, seeing or hearing things that are not real (hallucinations), unusual or disturbing thoughts (abnormal thinking), feeling anxious or upset, depression, thoughts of killing yourself or trying to kill yourself, increased tiredness, feelings of guilt or worthlessness and difficulty concentrating. Tell your doctor if you have or had depression or have tried to harm yourself. **Call your doctor right away if you have symptoms of mental health problems or a change in weight or appetite.**
- **Sleepwalking.** Sleepwalking can cause injuries. Call your doctor if you start sleepwalking.

Tell your doctor if you are on a salt-restricted diet or if you have high blood pressure, heart failure or kidney problems. LUMRYZ contains a lot of sodium (salt) and may not be right for you.

The most common side effects of LUMRYZ in adults include nausea, dizziness, bedwetting, headache and vomiting. Your side effects may increase when you take higher doses of LUMRYZ. LUMRYZ can cause physical dependence and craving for the medicine when it is not taken as directed. These are not all the possible side effects of LUMRYZ.

For more information, ask your doctor or pharmacist. Call your doctor for medical advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information, including BOXED Warning.

Cautionary Disclosure Regarding Forward-Looking Statements

This press release includes "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects or other events. Such forward-looking statements include, but are not limited to, expectations regarding the potential therapeutic benefit of and market preference for LUMRYZ in idiopathic hypersomnia, if approved; the progress, timing and success of the Phase 3 REVITALYZ trial, including expectations for trial design and enrollment; and statements regarding the results and analysis of Avadel's trials and studies including the details and content thereof. In some cases, forward-looking statements can be identified by the use of words such as "will," "may," "could," "believe," "expect," "look forward," "on track," "guidance," "anticipate," "estimate," "project," "next steps" and similar expressions and the negatives thereof (if applicable).

The Company's forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company's business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company's business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company's forward-looking

statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of the Company's Annual Report on Form 10-K for the year ended December 31, 2023, which was filed with the Securities and Exchange Commission (SEC) on February 29, 2024, and subsequent SEC filings. Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.

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EXHIBIT 9



Original Investigation | Health Policy

Characteristics of Clinical Studies Used for US Food and Drug Administration Supplemental Indication Approvals of Drugs and Biologics, 2017 to 2019

Meera Dhodapkar, BA; Audrey D. Zhang, MD; Jeremy Puthumana, MD, MS; Nicholas S. Downing, MD; Nilay D. Shah, PhD; Joseph S. Ross, MD, MHS

Abstract

IMPORTANCE After US Food and Drug Administration (FDA) approval of a new drug, sponsors can submit additional clinical data to obtain supplemental approval for use for new indications.

OBJECTIVE To characterize pivotal trials supporting recent supplemental new indication approvals of drugs and biologics by the FDA and to compare them with pivotal trials that supported these therapeutics' original indication approvals.

DESIGN, SETTING, AND PARTICIPANTS This is a cross-sectional study characterizing pivotal trials supporting supplemental indication approvals by the FDA between 2017 and 2019 and pivotal trials that supported these therapeutics' original indication approvals. Data analysis was performed from August to October 2020.

MAIN OUTCOMES AND MEASURES Number and design of pivotal trials supporting both supplemental and original indication approvals.

RESULTS From 2017 to 2019, the FDA approved 146 supplemental indications for 107 therapeutics on the basis of 181 pivotal efficacy trials. The median (interquartile range) number of trials per supplemental indication was 1 (1-1). Most trials used either placebo (77 trials [42.5%; 95% CI, 35.6%-49.8%]) or active comparators (65 trials [35.9%; 95% CI, 29.3%-43.1%]), and most of these multigroup trials were randomized (141 trials [99.3%; 95% CI, 96.0%-100.0%]) and double-blinded (106 trials [74.5%; 95% CI, 66.6%-81.0%]); 80 trials (44.2%; 95% CI, 37.2%-51.5%) used clinical outcomes as the primary efficacy end point. There was no difference between oncology therapies and those approved for other therapeutic areas to have supplemental indication approvals be based on at least 2 pivotal trials (11.5% vs 20.6%; difference, 9.1%; 95% CI, 2.9%-21.0%; $P = .10$). Similarly, there was no difference in use of randomization (98.3% vs 100.0%; difference, 1.7%; 95% CI, 1.6%-5.0%; $P = .43$) among multigroup trials, although these trials were less likely to be double-blinded (50.8% vs 92.3%; difference, 41.5%; 95% CI, 27.4%-55.5%; $P < .001$); overall, these trials were less likely to use either placebo or active comparators (64.9% vs 86.7%; difference, 21.8% 95% CI, 9.8%-33.9%; $P < .001$) or to use clinical outcomes as their primary efficacy end point (27.5% vs 61.1%; difference, 33.6%; 95% CI, 14.1%-40.9%; $P < .001$) and were longer (median [interquartile range], 17 [6-48] weeks vs 95 [39-146] weeks). Original approvals were more likely than supplemental indication approvals to be based on at least 2 pivotal trials (44.0% [95% CI, 33.7%-42.6%] vs 15.8% [95% CI, 10.7%-22.5%]; difference, 28.2%; 95% CI, 17.6%-39.6%; $P < .001$) and less likely to be supported by at least 1 trial of 12 months' duration (27.6% [95% CI, 17.9%-35.0%] vs 54.8% [95% CI, 46.7%-62.6%]; difference, 27.2%; 95% CI, 14.5%-37.8%; $P < .001$). Pivotal trial designs were otherwise not significantly different.

CONCLUSIONS AND RELEVANCE These findings suggest that the number and design of the pivotal trials supporting supplemental indication approvals by the FDA varied across therapeutic areas, with

(continued)

Key Points

Question What is the strength of evidence supporting supplemental new indication approvals for drugs and biologics and how does it compare with the evidence that supported their original approval?

Findings In this cross-sectional study of 107 therapeutics approved for 146 supplemental indications by the US Food and Drug Administration between 2017 and 2019, supplemental approvals for oncology drugs were based on fewer pivotal efficacy trials with less rigorous designs than supplemental approvals for other therapeutic areas. Supplemental approvals were based on fewer pivotal trials than their original indication approvals, but their designs were similar.

Meaning These findings suggest that there was little difference in the evidence supporting supplemental and original indication approvals, but the number and design of pivotal trials supporting supplemental indication approvals varied according to therapeutic area.

Author affiliations and article information are listed at the end of this article.

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Abstract (continued)

the strength of evidence for cancer indications weaker than that for other indications. There was little difference in the design characteristics of the pivotal trials supporting supplemental indication and original approvals.

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Introduction

To receive US Food and Drug Administration (FDA) approval for a new small-molecule or biologic drug, sponsors must submit “adequate and well controlled investigations”¹ to demonstrate the drug’s efficacy and safety. Although the FDA suggests that sponsors submit at least 2 trials demonstrating efficacy, also known as pivotal efficacy trials, the number and characteristics of pivotal efficacy trials supporting new drug and biologic approvals vary widely.^{2,3} For example, approximately one-third of new approvals are based on a single pivotal trial, whereas nearly one-half are based on trials solely focused on surrogate markers of disease, as opposed to clinical outcomes.² This flexibility highlights the FDA’s ability to adapt its standards to the clinical context and use of the drug or biologic under consideration.⁴

Less is known about the clinical trial evidence that supports supplemental indication approvals by the FDA, which are required when sponsors intend to add use of the originally approved drug for new clinical indications or in specific subpopulations to the labeling. Supplemental indication approvals by the FDA for already marketed drugs occur in frequencies similar to those for approvals for novel therapeutics. For instance, in 2014, the FDA approved 40 new supplemental indications compared with 44 new drug approvals.⁵ Supplemental new indication approvals are particularly common among oncology therapies, such as the anti-programmed death-1 biologic pembrolizumab (Keytruda), which was originally approved for the treatment of advanced melanoma in 2014 and has since been approved for 19 additional clinical indications.⁶ Moreover, it is critical that both new and supplemental indication approvals are based on strong evidence, because certain therapeutics may be prescribed more often for their supplemental indications than for their initially approved indication.⁷ Supplemental indication approval by the FDA is also critical for ensuring insurance coverage, especially for more expensive biological therapies and those used for oncology, where effective treatment options may be more limited.⁸

There have been few studies characterizing the clinical trial evidence that supported supplemental indication approvals by the FDA. One study⁹ broadly examined nearly 300 supplemental indication approvals between 2005 and 2014 and found that approximately one-third used active comparator groups and one-third used clinical outcomes as primary end points. Another study¹⁰ examined new and supplemental indication approvals, as well as off-label indications included in a Medicare-referenced compendium in oncology, from 2005 to 2012 and found the number and characteristics of supporting pivotal trials to be similar. However, whether recent supplemental indication approvals differ from original approvals more broadly and whether the evidentiary standards required for a supplemental indication approval for oncology therapeutics differ from those required for other therapeutics remain unknown. This information is particularly important in the context of ongoing efforts to increasingly leverage observational studies, as opposed to clinical trials, to support regulatory evaluations and supplemental indication approvals, including federal legislation like the 21st Century Cures Act.

Accordingly, we reviewed all supplemental new drug applications (sNDAs) and supplemental biologics license applications (sBLAs) approved by the FDA for new clinical indications from 2017 to 2019 to describe the characteristics of the pivotal efficacy clinical trials supporting their original indications and supplemental indications. We expect our findings will inform policy makers and clinician decision-making, particularly our understanding of the clinical evidentiary standards for supplemental new indication approvals.

Methods

This study was prepared in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cross-sectional studies. This study did not require institutional review board approval or informed consent because it was based on publicly available information and involved no patient records, in accordance with 45 CFR §46.

Sample Construction

One study author (M.D.) identified all new drugs and biologics approved for supplemental indications between January 2017 and December 2019 using the Drugs@FDA database. We limited our sample to sNDAs and sBLAs approved by the FDA for new clinical indications, identified through full-text review of sNDA and sBLA approval letters; corresponding FDA approval letters and printed labels were obtained as they are hyperlinked in the Drugs@FDA database. Duplicate records were removed, and sNDAs and sBLAs for contrast agents, nontherapeutic agents, and generics and biosimilars were excluded. Furthermore, we excluded any sBLAs that were determined to be (original) BLAs and removed from FDA's Orange Book on March 23, 2020, under the Biologics Price Competition and Innovation Act of 2009. Next, for each therapeutic for which an sNDA or sBLA was identified and included in our study, we identified the original indication NDA or BLA approved by the FDA, along with the pivotal trials supporting the FDA's approval for their original indication using previously described methods.^{2,3}

Supplemental Indication and Regulatory Characteristics

New indication approvals and original indication approvals were characterized by agent type, therapeutic area, and special regulatory status. For each approval, we determined whether the approved therapeutic was a small molecule or biologic from the letter and label. Treatments were characterized as short-term if the therapeutics were expected to be used for less than 1 month, as intermediate if they were expected to be used for 1 month to 2 years, and long-term if they were expected to be used for more than 2 years. Therapeutic area was classified for each approval was based on the World Health Organization Anatomical Therapeutic Classification System.¹¹ Using publicly available information on the FDA website, we determined whether each indication in our sample was evaluated under a special regulatory program such as Priority Review,¹² Accelerated Approval,¹³ Fast Track¹⁴ for (NDAs and BLAs only), or Breakthrough Therapy.¹⁵

Trial Identification

To identify the pivotal clinical trials supporting the sNDAs and sBLAs, we reviewed the drug labels updated by the FDA to correspond to the specific new indication approval, which typically reference the clinical trial using the ClinicalTrials.gov registration number (ie, National Clinical Trials identifier). Generally, those studies considered pivotal are labeled as such in the Clinical Studies section of the printed label. Furthermore, if not directly stated as pivotal, efficacy for an indication is stated to be based on the evidence from a trial or number of trials. If an approval was based on the results of more than 1 trial, all these trials were included in our study. To identify pivotal trials not directly referenced in the label using a National Clinical Trials number, general study information (eg, number of study participants, primary efficacy end point, masking, and randomization) was cross-referenced with study information from ClinicalTrials.gov to identify the relevant National Clinical Trials number.

Pivotal Trial Characterization

For all pivotal trials supporting NDA, sNDA, BLA, and sBLA approval by the FDA, 1 study author (M.D.) extracted the following information from ClinicalTrials.gov if not available from or previously collected as part of prior research from FDA action packages, including approval letters and review documents: randomization, double-blinding, comparator, study end point, agent type, total number of participants, and number of patients in intervention group.^{2,3} For each trial included in our sample,

we determined its use of randomization and double-blinding and characterized the comparator group as active, placebo, or none. Next, the primary trial end point was identified and was designated into 1 of 3 categories—clinical outcome, clinical scale, or surrogate marker—by 1 study author (M.D.) and was reviewed by another study author (J.S.R.); any conflicts were resolved by consensus. In brief, surrogate markers (eg, hemoglobin A_{1c}) are metrics expected to be associated with patient outcomes, where clinical outcomes (eg, death) measure patient outcomes. Importantly, if at least 1 primary trial end point was categorized as a clinical outcome or clinical scale, the trial would be categorized as such even if another primary trial end point was a surrogate marker. The number of participants, intervention model, and number of patients in the intervention group were also extracted. Trial duration was extracted from study descriptions using methods previously described.^{2,3} For time-associated end points, duration was defined as the date of measurement of the primary end point. For event-associated end points, duration was determined as the median follow-up time for participants or the weighted average of the median follow-up time in cases in which it differed between study groups.

Statistical Analysis

We used descriptive statistics to examine differences in trial characteristics and indication characteristics. Frequencies of use of randomization and double-blinding among the trials in our sample were calculated excluding single-group studies. We next used χ^2 and Wilcoxon tests where appropriate to examine differences between supplemental indication approvals for therapeutics in our sample at multiple levels, including agent type, special regulatory pathway, and therapeutic area, all of which were defined before data collection. Analyses were performed using R statistical software version 3.4.3 (R Project for Statistical Computing), JMP statistical software version 15.0.0 (SAS Institute), Python statistical software version 3.8 (Python), and Excel spreadsheet software version 16.16.27 (Microsoft). All statistical tests were 2-tailed and used a type I error rate of .01 to account for multiple comparisons. Data analysis was performed from August to October 2020.

Results

Between January 2017 and December 2019, the FDA approved 3721 new sNDA and sBLAs (3200 sNDAs and 521 sBLAs), among which were 146 supplemental indication approvals for a new clinical indication, for a total of 107 therapeutics. Among the 146 supplemental indication approvals, 99 (68%) were for pharmacologics and 47 (32%) were for biologics; 74 (51%) were approved using at least 1 special regulatory program, including 20 using the Accelerated Approval pathway and 61 designated for Priority Review (**Table 1**). Most commonly, the supplemental indication approvals were for the treatment of cancer (78 approvals [53%]) or autoimmune and musculoskeletal (24 approvals [16%]) disease.

Pivotal Trials Supporting Supplemental Indication Approvals

The FDA approved these 146 supplemental indications on the basis of 181 pivotal trials, with a median (interquartile range [IQR]) of 1 (1-1) trial per approval; 23 (15.8%) supplemental indication approvals were approved on the basis of at least 2 pivotal trials. Most pivotal trials supporting these indications used either an active (65 trials [35.9%; 95% CI, 29.3%-43.1%]) or placebo (77 trials [42.5%; 95% CI, 35.6%-49.8%]) comparator, and the majority of these multigroup trials were randomized (141 trials [99.3%; 95% CI, 96.0%-100.0%]) and double-blinded (106 trials [74.5%; 95% CI, 66.6%-81.0%]); 80 trials (44.2%; 95% CI, 37.2%-51.5%) used clinical outcomes as the primary efficacy end point (**Table 2**). The median (IQR) trial duration was 46.3 (16-117) weeks. The median (IQR) number of patients in the pivotal trials was 460 (226-734), and the median (IQR) number of patients in the intervention groups was 267 (149-473).

Supplemental Indication Approvals, Comparing Product Types

The 99 pharmacologic supplemental indication approvals were supported by 125 pivotal trials, whereas the 47 biologic approvals were supported by 56 trials (Table 2). The median (IQR) number of trials per approval was 1 (1-1) for pharmacologic approvals and 1 (1-1) for biologic approvals; 18 pharmacologic indications (18.2%) and 5 biologic indications (10.6%) were approved on the basis of at least 2 pivotal trials. Likewise, the trials supporting supplemental indication approvals were broadly similar in design between pharmacologics and biologics. Trials supporting pharmacologic approvals were as likely as trials supporting biologic approvals to be randomized (100.0% [95% CI, 96.4%-100.0%] vs 97.2% [95% CI, 85.5%-99.5%]; $P = .26$) and double-blind (77.5% [95% CI, 68.4%-84.5%] vs 65.7% [95% CI, 49.2%-79.2%]; $P = .18$) when multigrouped (106 trials for pharmacologic approvals and 36 trials for biologic approvals), and to use a clinical outcome as their primary efficacy end point (48.8% [95% CI, 42.5%-59.8%] vs 33.9% [95% CI, 22.9%-47.0%]; $P = .08$), but were more likely to have either an active or placebo comparator group (84.8% [95% CI, 77.5%-90.9%] vs 64.3% [95% CI, 51.2%-75.5%]; $P = .002$). The duration of trials supporting pharmacologic approvals did not differ from the duration of trials supporting biologic approvals (median [IQR], 40.7 [12.2-121.3] vs 47.1 [24-101.7] weeks). The number of overall patients in the pivotal trials (median [IQR] 518 [276-797.5] vs 305.5 [163.8-559] patients) and in the intervention groups (median [IQR], 304 [158-480] vs 223.5 [125-338] patients) did not differ between pharmacologic and biologic approvals.

When aggregating all the pivotal trials that supported the indication approval, the number of patients overall (median [IQR], 514 [269-834] vs 306 [157-713] patients) and in the intervention groups overall (median [IQR], 281.5 [155-451] vs 222 [105-340] patients) did not differ between pharmacologic and biologic approvals (Table 3). Pharmacologic and biologic approvals did not differ in there being at least 1 pivotal trial that was randomized (81.8% [95% CI, 73.1%-88.2%] vs 63.8% [95% CI, 49.5%-76.0%]; $P = .02$), double-blinded (65.7% [95% CI, 55.9%-74.3%] vs 44.7% [95% CI,

Table 1. Characteristics of Supplemental New Indication Drugs and Biologics Approved by the US FDA for New Indications from 2017 to 2019, and the New Drugs and Biologics Approved by the FDA for the Corresponding Original Indications

Characteristic	Approvals, No. (%)	
	Supplemental new indication (n = 146) ^a	Original (n = 109)
Approval year		
Before 2010	NA	23 (21)
2010-2014	NA	45 (41)
2015-2019	146 (100)	41 (38)
Agent type		
Pharmacologics	99 (68)	69 (63)
Biologics	47 (32)	40 (37)
Special regulatory program		
Any	74 (51)	57 (52)
Accelerated approval	20 (14)	25 (23)
Priority review	61 (42)	55 (50)
Fast track	NA	10 (9)
Breakthrough	35 (24)	17 (16)
Therapeutic area		
Autoimmune or musculoskeletal	24 (16)	5 (5)
Infectious diseases	5 (3)	6 (6)
Neurology	8 (5)	NA ^b
Dermatology	NA ^b	7 (6)
Cardiovascular, diabetes, and lipids	9 (6)	13 (12)
Cancer	78 (53)	46 (42)
Other	22 (15)	7 (6)

Abbreviations: FDA, US Food and Drug Administration; NA, not applicable.

^a Supplemental approvals are not eligible for Fast Track designation.

^b Therapeutic areas with fewer than 5 new indications or original indication approvals, respectively, are consolidated into the other category.

Table 2. Characteristics of Trials Supporting Supplemental New Indication Approvals by the US Food and Drug Administration Between 2017 and 2019

		Percentage (95% CI)						Patients, median (IQR), No.		
Characteristic	Trials, No.	Randomized ^a	Double-blind ^a	Comparator			Clinical end point	Trial duration, median (IQR), wk	Overall	Intervention group
				Placebo	Active	Single group				
Overall	181	99.3 (96.0-100.0)	74.6 (66.6-81.0)	42.5 (35.6-49.8)	35.9 (29.3-43.1)	21.6 (16.2-28.1)	44.2 (37.2-51.5)	46.3 (16-117)	460 (226-734)	267 (148.5-473)
Agent type										
Pharmacologic sNDAs	125	100.0 (96.4-100.0)	77.5 (68.4-84.5)	46.4 (37.9-55.1)	38.4 (30.3-47.2)	15.2 (9.9-22.5)	48.8 (42.5-59.8)	40.7 (12.2-121.3)	518 (276-797.5)	304 (158-480)
Biologic sBLAs	56	97.2 (85.5-99.5)	65.7 (49.2-79.2)	33.9 (22.9-47.0)	30.4 (19.9-43.3)	35.7 (24.5-48.8)	33.9 (22.9-47.0)	47.1 (24-101.7)	305.5 (163.8-559)	223.5 (125-338)
P value		.26	.18	.002	.002	.002	.08	.71	.02	.10
Special regulatory pathway										
Any	87	98.2 (90.2-99.7)	59.4 (46.0-71.3)	28.7 (20.3-39.0)	37.9 (28.5-48.4)	33.3 (24.3-43.8)	32.2 (23.3-42.6)	62.1 (30-128.6)	450 (207-726)	271 (149-444)
Accelerated approval	25	87.5 (52.9-97.8)	37.5 (13.7-69.4)	12.0 (4.2-30.0)	24.0 (11.5-43.4)	64.0 (44.5-79.8)	24.0 (11.5-43.4)	52.7 (34.1-107.4)	340 (177.5-743)	270 (152-424)
Priority review	74	97.9 (89.1-99.6)	64.6 (50.4-76.6)	33.8 (24-45.1)	36.5 (26.4-47.9)	29.7 (20.5-40.9)	32.4 (22.9-43.7)	56.4 (30-129)	449 (207.8-706.25)	256 (149.8-439.5)
Breakthrough	44	100 (85.1-100)	45.5 (26.9-65.3)	13.6 (6.4-26.7)	40.9 (27.7-55.6)	45.5 (31.7-59.9)	18.2 (9.5-31.9)	100.5 (42.1-128.9)	448.5 (206.2-710.8)	319.5 (159.5-319.5)
P value (any special regulatory program vs none)		.39	<.001	<.001	<.001	<.001	.02	.001	.004	.07
Therapeutic area										
Autoimmune or musculoskeletal	36	100 (89.3-100)	96.9 (84.3-99.4)	69.44 (53.1-82.0)	22.2 (11.7-38.1)	8.3 (2.9-21.8)	66.7 (50.3-79.8)	24 (14.5-25.7)	329 (188-546)	212.5 (104.3-344)
Cancer	91	98.3 (91.0-99.7)	50.8 (38.4-63.2)	23.1 (15.6-32.7)	41.8 (32.2-52.0)	35.2 (26.1-45.4)	27.5 (19.4-37.4)	94.9 (38.6-145.7)	501 (292-737)	297 (196-476)
Cardiovascular, diabetes, or lipids	11	100 (74.1-100)	100 (74.1-100)	54.6 (28.0-78.7)	45.5 (21.3-72)	0	81.8 (52.3-94.9)	100.3 (5.1-134.3)	4541 (2531-9341)	2266 (1252-4668)
Infectious diseases	6	100 (61.0-100)	66.7 (30.0-90.3)	16.7 (3.0-56.4)	83.3 (43.6-97.0)	0	66.7 (30.0-90.3)	3.8 (1-48)	621.5 (448-887.3)	311.5 (213.8-414.5)
Neurology	9	100 (67.6-100)	100 (67.5-100)	77.8 (45.3-93.7)	11.1 (2.0-43.5)	11.1 (2.0-43.5)	66.7 (35.4-87.9)	4 (4-6)	212 (146.5-375)	155 (89.5-251.5)
Other	28	100 (84.5-100)	85.7 (65.4-95.0)	57.1 (39.1-73.5)	21.4 (10.2-39.5)	21.4 (10.2-39.5)	42.9 (26.5-60.9)	18.5 (6-52)	291 (106.8-699.8)	199 (99-433.3)
P value (oncology v nononcology)		.43	<.001	<.001	<.001	<.001	<.001	<.001	.62	.88

Abbreviations: IQR, interquartile range; sBLA, supplemental biologics license application; sNDA, supplemental new drug application.

^a Excludes single-group studies.

31.4%-58.8%]; $P = .02$), used a clinical outcome as the primary efficacy end point (51.5% [95% CI, 41.8%-61.1%] vs 31.9% [95% CI, 20.4%-46.2%]; $P = .03$), and had a duration of at least 6 months (66.7% [95% CI, 56.9%-75.2%] vs 72.3% [95% CI, 58.2%-83.1%]; $P = .49$) or 12 months (54.6% [95% CI, 44.8%-64.0%] vs 55.3% [95% CI, 41.2%-68.6%]; $P = .93$), but pharmacologic approvals were more likely to have at least 1 pivotal trial that used either an active or placebo comparator (84.8% [95% CI, 76.5%-90.6%] vs 66.0% [95% CI, 51.7%-77.8%]; $P = .009$) (**Table 4**).

Supplemental Indication Approvals, Comparing Therapeutic Areas

The 78 oncology supplemental indication approvals were supported by 91 pivotal trials, whereas the 68 nononcology approvals were supported by 90 pivotal trials (Table 2). The median (IQR) number of trials per approval was 1 (1-1) and 1 (1-1), respectively, and 9 oncology indications (11.5%) and 14 nononcology indications (20.6%) were approved on the basis of at least 2 pivotal trials (difference,

Table 3. Number and Characteristics of Aggregated Pivotal Efficacy Trials Providing the Basis for Original and Supplemental Indication Approvals by the US Food and Drug Administration Between 2017 and 2019, Stratified by Supplemental or Original Indication, Therapeutic Agent, and Indication Characteristics

Variable	Trials, No.	Pivotal efficacy trials, median (IQR), No.	Patients in aggregated pivotal efficacy trials, median (IQR), No.	
			Overall	Intervention group
Supplemental or original indication				
Original	109	1 (1-2)	326 (161.5-676)	256.3 (120.1-375.4)
Supplemental	146	1 (1-1)	445 (211.8-799.3)	256.5 (144.8-447.3)
P value		<.001	.05	.12
Therapeutic agent				
Pharmacologic sNDA	99	1 (1-1)	514 (269-834)	281.5 (155-451)
Biologic sBLA	47	1 (1-1)	306 (157-713)	222 (105-340)
P value		.26	.05	.16
Therapeutic area				
Oncology sNDA or sBLA	78	1 (1-1)	505 (300.8-873)	286 (200-471.5)
Nononcology sNDA or sBLA	68	1 (1-1)	334.3 (153.3-749.8)	215.5 (99-421)
P value		.13	.06	.04

Abbreviations: IQR, interquartile range; sBLA, supplemental biologics license applications; sNDA, supplemental new drug application.

Table 4. Proportion of Indication-Level Approvals of Novel Therapeutic Agents by the US Food and Drug Administration on the Basis of at Least 1 Trial That Met the Criteria Below, Stratified by Supplemental or Original Indication, Therapeutic Agent, and Indication Characteristics

		Percentage (95% CI)						
Variable	Trials, No.	≥2 Pivotal trials	≥1 Randomized trial	≥1 Double-blind trial	Trial duration		≥1 Trial	With clinical outcome as primary efficacy end point
					≥6 mo	≥12 mo	With active or placebo comparator	
Supplemental or original indication								
Original	109	44.0 (33.7-42.6)	80.0 (71.4-86.5)	63.8 (54.3-72.4)	51.5 (43.3-62.6)	27.6 (17.9-35.0)	78.8 (70.0-85.6)	53.9 (46.2-65.0)
Supplemental	146	15.8, (10.7-22.5)	76.0 (68.5-82.2)	58.9 (50.8-66.6)	68.5 (60.6-75.5)	54.8 (46.7-62.6)	78.9 (71.4-84.6)	45.2 (37.4-53.3)
P value		<.001	.54	.51	.01	<.001	.87	.18
Therapeutic area								
Pharmacologic sNDA	99	18.2 (11.8-26.9)	81.8 (73.1-88.2)	65.7 (55.9-74.3)	66.7 (56.9-75.2)	54.6 (44.8-64.0)	84.8 (76.5-90.6)	51.5 (41.8-61.1)
Biologic sBLA	47	10.6 (4.6-22.6)	63.8 (49.5-76.0)	44.7 (31.4-58.8)	72.3 (58.2-83.1)	55.3 (41.2-68.6)	66.0 (51.7-77.8)	31.9 (20.4-46.2)
P value		.24	.02	.02	.49	.93	.009	.03
Therapeutic area								
Oncology sNDA or sBLA	78	11.5 (6.2-20.5)	68.8 (57.9-77.8)	37.5 (27.7-48.5)	93.6 (85.9-97.2)	76.9 (66.4-84.9)	71.9 (61-80.6)	32.1 (22.7-43.0)
Nononcology sNDA or sBLA	68	20.6 (12.7-31.6)	84.8 (74.3-91.6)	84.8 (74.3-91.6)	39.7 (28.9-51.6)	29.4 (19.9-41.1)	86.8 (76.7-92.9)	60.3 (48.4-71.1)
P value		.10	.04	<.001	<.001	<.001	.03	<.001

Abbreviations: sBLA, supplemental biologics license application; sNDA, supplemental new drug application.

9.1%; 95% CI, 2.9%-21.0%; $P = .10$). The trials supporting therapeutics used for oncology indications did not differ significantly from the trials supporting indications used for all other therapeutic areas with respect to use of randomization (98.3% vs 100.0%; difference, 1.7%; 95% CI, 1.6%-5.0%; $P = .43$), but were significantly less likely to be double-blinded (50.8% vs 92.3%; difference, 41.5%; 95% CI, 27.4%-55.5%; $P < .001$) when multigrouped (59 oncology trials and 78 nononcology trials); overall, these trials were less likely to use either a placebo or active comparator group (64.9% vs 86.7%; difference, 21.8%; 95% CI, 9.8%-33.9%; $P < .001$) and to use clinical outcomes as their primary efficacy end point (27.5% vs 61.1%; difference, 33.6%; 95% CI, 14.1%-40.9%; $P < .001$). However, trials supporting oncology indications were longer than trials supporting indications in all other therapeutic areas (median [IQR], 95 [39-146] weeks vs 17 [6-48] weeks). The number of overall patients the pivotal trials (median [IQR], 501 [292-737] vs 393.5 [203-747] patients) and in the intervention groups (median [IQR], 297 [196-476] vs 243 [104.8-449.3] patients) did not differ between trials supporting oncology indications and indications in all other therapeutic areas.

When aggregating all the pivotal trials that supported the indication approval, the number of patients overall (median [IQR], 505 [300.8-873] vs 334.3 [153.3-749.8] patients) and in the intervention groups (median [IQR], 286 [200-471.5] vs 215.5 [99-421] patients) did not differ between oncology and nononcology approvals (Table 3). Oncology approvals were not less likely to be supported by at least 1 pivotal trial that was randomized (68.8% [95% CI, 57.9%-77.8%] vs 84.8% [95% CI, 74.3%-91.6%]; $P = .04$) or used either an active or placebo comparator (71.9% [95% CI, 61.0%-80.6%] vs 86.8% [95% CI, 76.7%-92.9%]; $P = .03$), but were less likely to be supported by at least 1 trial that was double-blinded (37.5% [95% CI, 27.7%-48.5%] vs 84.8% [95% CI, 74.3%-91.6%]; difference, 47.3%; 95% CI, 33.9%-61.3%; $P < .001$) and that used a clinical outcome as the primary efficacy end point (32.1% [95% CI, 22.7%-43.0%] vs 60.3% [95% CI, 48.4%-71.1%]; difference, 28.2%; 95% CI, 12.7%-43.8%; $P < .001$), and were more likely to be supported by at least 1 trial that had a duration of at least 6 months (93.6% [95% CI, 85.9%-97.2%] vs 39.7% [95% CI, 28.9%-51.6%]; difference, 53.9%; 95% CI, 41.0%-66.7%; $P < .001$) or 12 months (76.9% [95% CI, 66.4%-84.9%] vs 29.4% [95% CI, 19.9%-41.1%]; difference, 47.5%; 95% CI, 33.2%-61.8%; $P < .001$) (Table 4).

Supplemental Indication Approvals Compared With Original Indication Approvals

The 107 therapeutics for which we identified supplemental indication approvals were originally approved by the FDA for 109 clinical indications (Table 1); original indication approvals took place between 1991 and 2018, and 18% (19 of 107 approvals) were approved for a supplemental indication in a different therapeutic area from the original indication approval, the majority of which (11 approvals) were approved for a supplemental indication for use for autoimmune or musculoskeletal disease after an original approval for a different clinical use. The median (IQR) number of trials per approval was 1 (1-2) and 1 (1-1), respectively (Table 3); original indication approvals were significantly more likely to be supported by at least 2 pivotal efficacy trials compared with supplemental indication approvals (44.0% [95% CI, 33.7%-42.6%] vs 15.8% [10.7%-22.5%]; difference, 28.2%; 95% CI, 17.6%-39.6%; $P < .001$). There was no difference between original and supplemental indication approvals with respect to being supported by at least 1 pivotal trial that was randomized (80.0% [95% CI, 71.4%-86.5%] vs 76.0% [95% CI, 68.5%-82.2%]; $P = .54$), double-blinded (63.8% [95% CI, 54.3%-72.4%] vs 58.9% [95% CI, 50.8%-66.6%]; $P = .51$), used either an active or placebo comparator (78.8% [95% CI, 70.0%-85.6%] vs 78.9% [95% CI, 71.4%-84.6%]; $P = .87$), and used a clinical outcome as the primary efficacy end point (53.9% [95% CI, 46.2%-65.0%] vs 45.2% [95% CI, 37.4%-53.3%]; $P = .18$); however, original indication approvals were significantly less likely to be supported by at least 1 trial that had a duration of at least 6 months (51.5% [95% CI, 43.3%-62.6%] vs 68.5% [95% CI, 60.6%-75.5%]; difference, 17.0%; 95% CI, 3.7%-27.8%; $P = .01$) or 12 months (27.6% [95% CI, 17.9%-35.0%] vs 54.8% [95% CI, 46.7%-62.6%]; difference, 27.2%; 95% CI, 14.5%-37.8%; $P < .001$) (Table 4). There was no difference between original and supplemental indication approvals with respect to the number of patients in the aggregated pivotal trials overall (median [IQR], 326

[62-676] vs 445 [162-676] patients) or the number in the intervention groups (median [IQR], 256 [120-375] vs 257 [145-447] patients).

Discussion

Among all supplemental new indications approved by the FDA between 2017 and 2019, we found that the number and design of the pivotal trials supporting supplemental indication approvals varied on the basis of therapeutic area, with the strength of evidence for cancer indications weaker than those for other indications. However, there was little difference in the number and design of the pivotal trials supporting pharmacologic and biologic supplemental indication approvals, or between supplemental and original indication approvals by the FDA. These findings suggest that the evidentiary standards for supplemental new indication approvals varies across therapeutic areas but that the FDA's standard for approval is consistent between supplemental and original indications for use.

Our study suggests that the trials supporting supplemental indication approvals for oncology therapeutics vary significantly from those trials supporting indications in all other therapeutic areas, with a tendency to be fewer in number and less robust in design compared with trials supporting supplemental approvals for indications in all other therapeutic areas. This variation highlights the flexible approach taken by the FDA, guided by the severity of the disease and availability of treatment alternatives. Flexible standards, with greater laxity for oncology approvals, was previously demonstrated in our study² characterizing the pivotal efficacy trials supporting original indication approval of novel therapeutics. In addition, substantial variation has been described with regard to the pivotal efficacy trials supporting the approval of novel oncology therapeutics.¹⁶

The evidentiary standard for supplemental new indication approval has important implications for clinical care and regulatory decision-making, offering insight into whether the FDA follows the precedent set by the therapeutic's original approval or whether a lower, or even a higher, standard is used. There are competing reasons for why the FDA might adopt a different standard for supplemental approvals. On the one hand, if safety was established through the agency's original approval, some might argue that additional trials are not needed for other clinical uses. Instead, safety may be inferred from prior use. This scenario plays out frequently through off-label prescribing of approved drugs and biologics, as reported by 21% of office-based physicians¹⁷ and as occurs among 80% of inpatient episodes of care among certain subpopulations, such as children.¹⁸ As opposed to physicians prescribing therapies off-label, with little to no evidence, perhaps regulatory standards could be lowered to incentivize any postmarket clinical evidence generation for new clinical uses after original approval.¹⁹

On the other hand, there is an argument that standards could be strengthened once a therapeutic is available for widespread use. The FDA could require larger and longer duration trials to more fully characterize longer-term risks of approved therapeutics, and this higher standard approach could preclude the use of surrogate markers as primary trial end points. Thus, the FDA could require more robust clinical trial designs to demonstrate drug safety and efficacy that would better inform physician-patient decision-making and coverage decisions. For more expensive therapies, supplemental new indication approval by the FDA generally guarantees insurance coverage for that therapeutic use, as opposed to broad coverage of the therapeutic for any use. For instance, the Centers for Medicare & Medicaid Services provides coverage of oncology drugs for any FDA-approved indication for use, as well as any off-label use listed in certain compendia, facilitating patient access even while supplemental indications are tested by sponsors and evaluated by the FDA.

Our findings suggest that the FDA maintains consistent evidentiary standards for both supplemental new and original indication approvals. However, ongoing efforts to increasingly leverage observational studies to support regulatory evaluations and approvals, as opposed to clinical trials, may affect these standards. The 21st Century Cures Act, which was signed into law on December 13, 2016, contains a provision to promote the use of real-world evidence (RWE)—that is,

studies of drugs and biologics that are derived from data collected in routine medical settings. In response, the FDA launched an initiative to explain the agency's former use of RWE for safety evaluations and plans for future uses,²⁰ including for supplemental new indication approvals.²¹ Even before this legislation, the FDA had used RWE to inform approvals, such as in 2014, when blinatumomab (Blinicyto) received accelerated approval by the FDA for the treatment of relapsed or refractory, Philadelphia chromosome-negative, acute lymphoblastic leukemia on the basis of a single-group, open-label phase 2 study. In this case, RWE came in the form of historical controls who received standard of care, and efficacy was shown according to a weighted analysis of data from medical record reviews.²²

Generating additional drug safety and effectiveness evidence through observational research may offer advantages with respect to time and resources, compared with clinical trials. However, there are outstanding issues to resolve, including data definitions, establishing which data are fit for purpose, and establishing best practices,²³ such as study registration.²⁴ Furthermore, our recent study²⁵ found that few of the recently published, highest-impact trials could be feasibly replicated using RWE because much of the data needed for randomized clinical trials are not captured in electronic health records in a structured format, if at all. Although the strengths and limitations of using RWE for the evaluation of supplemental new indication approvals for therapeutics already available for use are better characterized, there is a clear opportunity to complement randomized clinical trials to offer more information on product safety and efficacy.

Limitations

Our study has some limitations. First, we only assessed a recent, 3-year sample of therapeutics approved by the FDA for supplemental new clinical indications and, therefore, could not capture long-term trends in supplemental indication approvals or supplemental indication approvals by other national regulators. Second, our study did not evaluate whether the FDA considered other data regarding use of these therapeutics in other countries, which may have informed the agency's efforts to evaluate supplemental new indication approval safety and efficacy.

Conclusions

In this cross-sectional study, we found that there was little difference in the evidence supporting supplemental and original indication approvals by the FDA, but the number and design of pivotal trials supporting supplemental indication approvals varied according to therapeutic area, with the strength of evidence for cancer indications weaker than that for other indications. Overall, our results highlight the need for ongoing postmarket evaluation of supplemental new indications to ensure our understanding of product benefit and safety, as well as to inform both clinicians' and policy makers' decisions, including ongoing efforts to leverage observational studies and RWE, as opposed to clinical trials, to support FDA regulatory decisions and evaluations.

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Author Contributions: Ms Dhodapkar and Dr Ross had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Acquisition, analysis, or interpretation of data: All authors.

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Administrative, technical, or material support: Dhodapkar, Puthumana.

Supervision: Ross.

Conflict of Interest Disclosures: Ms Dhodapkar reported receiving grants from Yale School of Medicine Medical Student Summer Fellowship outside the submitted work. Dr Zhang reported receiving research support through the Collaboration for Research Integrity and Transparency at Yale University from the Laura and John Arnold Foundation. Dr Shah reported receiving research support through Mayo Clinic from the Food and Drug Administration, the Centers of Medicare & Medicaid Innovation under the Transforming Clinical Practice Initiative, the Agency for Healthcare Research and Quality (grants R01HS025164, R01HS025402, R03HS025517, and K12HS026379), the National Heart, Lung and Blood Institute of the National Institutes of Health (grants R56HL130496, R01HL131535, and R01HL151662), the National Science Foundation, the Medical Device Innovation Consortium as part of the National Evaluation System for Health Technology, and the Patient-Centered Outcomes Research Institute to develop a Clinical Data Research Network. Dr Ross reported receiving grants from Food and Drug Administration, Johnson & Johnson, Medical Devices Innovation Consortium, Agency for Healthcare Research and Quality, National Heart, Lung and Blood Institute of the National Institutes of Health, and the Laura and John Arnold Foundation outside the submitted work. No other disclosures were reported.

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Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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EXHIBIT 10



▶ —

AVADEL

Pharmaceuticals plc

(NASDAQ: AVDL)

A BIOPHARMACEUTICAL COMPANY FOCUSED ON TRANSFORMING MEDICINES TO TRANSFORM LIVES



Safe Harbor Statements

This presentation may include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. These forward-looking statements relate to our future expectations, beliefs, plans, strategies, objectives, results, conditions, financial performance, prospects or other events. Such forward-looking statements include, but are not limited to, expectations regarding the potential therapeutic benefit of LUMRYZ; the success of the commercialization of LUMRYZ and expansion into additional patient populations; the anticipated market demand and sales opportunity of LUMRYZ; the potential for the Company to be a leader in the market; the Company's idiopathic hypersomnia clinical study for LUMRYZ, including enrollment and timing related thereto; the potential development and related timing of a once-nightly, no-/low-sodium oxybate formulation; and the Company's anticipated financial condition, expenses, uses of capital and other future financial results. In some cases, forward-looking statements can be identified by use of words such as "will," "may," "could," "believe," "expect," "look forward," "on track," "guidance," "anticipate," "estimate," "project," "next steps" and similar expressions and the negatives thereof (if applicable).

The Company's forward-looking statements are based on estimates and assumptions that are made within the bounds of our knowledge of our business and operations and that we consider reasonable. However, the Company's business and operations are subject to significant risks, and, as a result, there can be no assurance that actual results and the results of the company's business and operations will not differ materially from the results contemplated in such forward-looking statements. Factors that could cause actual results to differ from expectations in the Company's forward-looking statements include the risks and uncertainties described in the "Risk Factors" section of Part I, Item 1A of the Company's most recent Annual Report on Form 10-K and subsequent filings with the Securities and Exchange Commission.

Forward-looking statements speak only as of the date they are made and are not guarantees of future performance. Accordingly, you should not place undue reliance on forward-looking statements. The Company does not undertake any obligation to publicly update or revise our forward-looking statements, except as required by law.



**Founded as an R&D company
over 30 years ago**

Within the last five years, Avadel has evolved into a strong commercial organization, delivering LUMRYZ™, a next-generation solution that fundamentally addresses the patient experience for People with Narcolepsy



Proprietary Formulation

LUMRYZ for patients 7 years and older:
*“enabling better nights for better days for
People with Narcolepsy”*

Publicly traded on
NASDAQ since 1996



~\$250M Revenue Since Launch*



~2,800

Patients on therapy*

Corporate Headquarters



Dublin, Ireland

US Operations

St. Louis,
Missouri



Deep, wholly-owned pipeline with
numerous expansion opportunities

30 Orange book listed patents
with expirations to early-2042

Management team with extensive
commercial experience in **rare and
orphan** drug launches

OUR VALUES



Relentless



Confidence
with Humility



Courageous

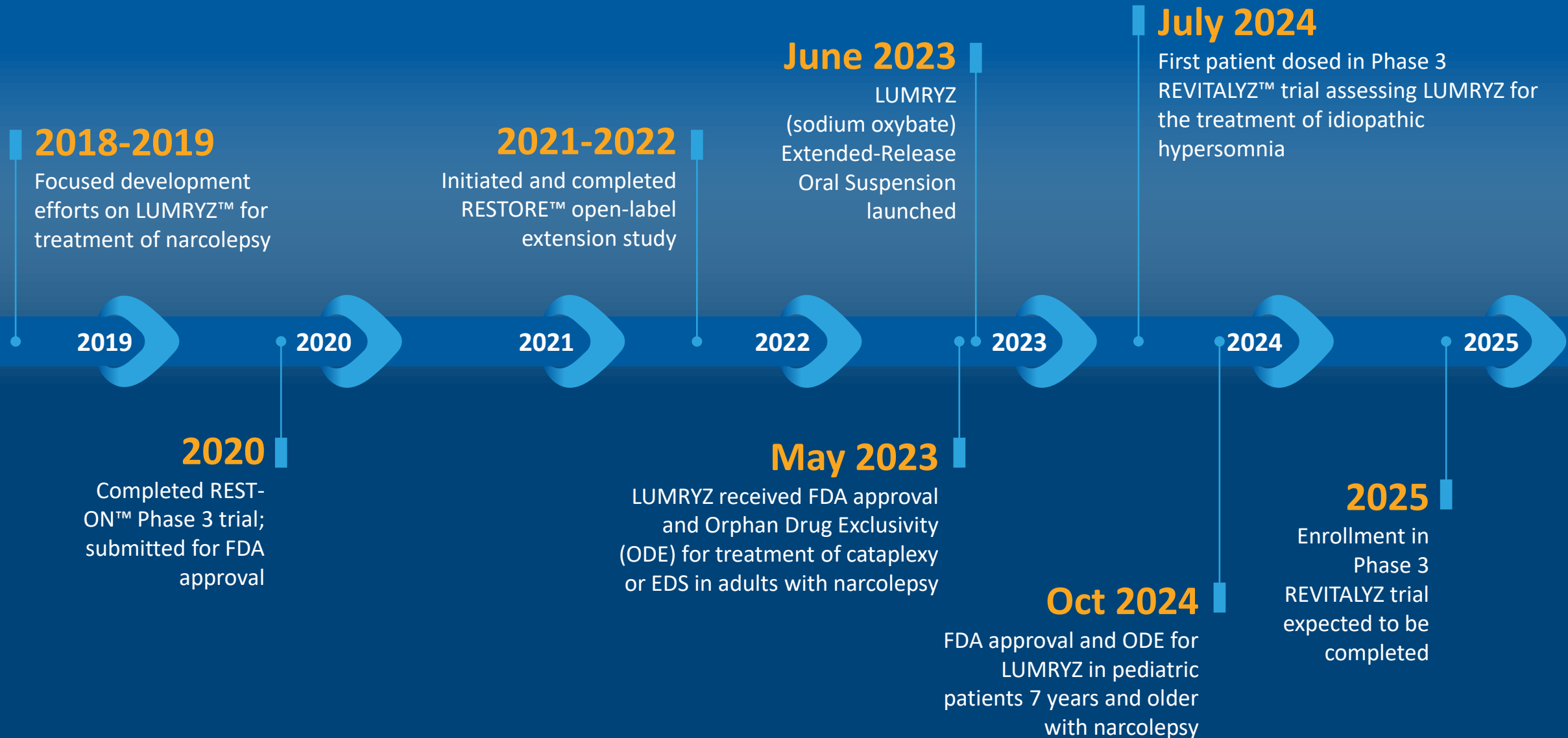


Insights
to Impact



Togetherness





Advancing Innovative and Transformative Sleep Medicine Pipeline

PROGRAM	INDICATION	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	REGULATORY REVIEW	COMMERCIAL	MAJOR MILESTONES
Sodium Oxybate Extended-Release Oral Suspension (LUMRYZ™)	Narcolepsy – Excessive Daytime Sleepiness (EDS) and/or Cataplexy in Adults							Received FDA approval and ODE in May 2023; launched in June 2023
	Narcolepsy - EDS and/or Cataplexy in Pediatrics Age 7+							Received FDA approval and ODE in October 2024
	Idiopathic Hypersomnia (IH)							First patient dosed in REVITALYZ™ Ph3 trial in July 2024
Extended-Release, No Sodium Oxybate Formulation	EDS and/or Cataplexy in Narcolepsy; IH							PK only development plan bio equivalent to LUMRYZ; estimated FDA approval 2H2027



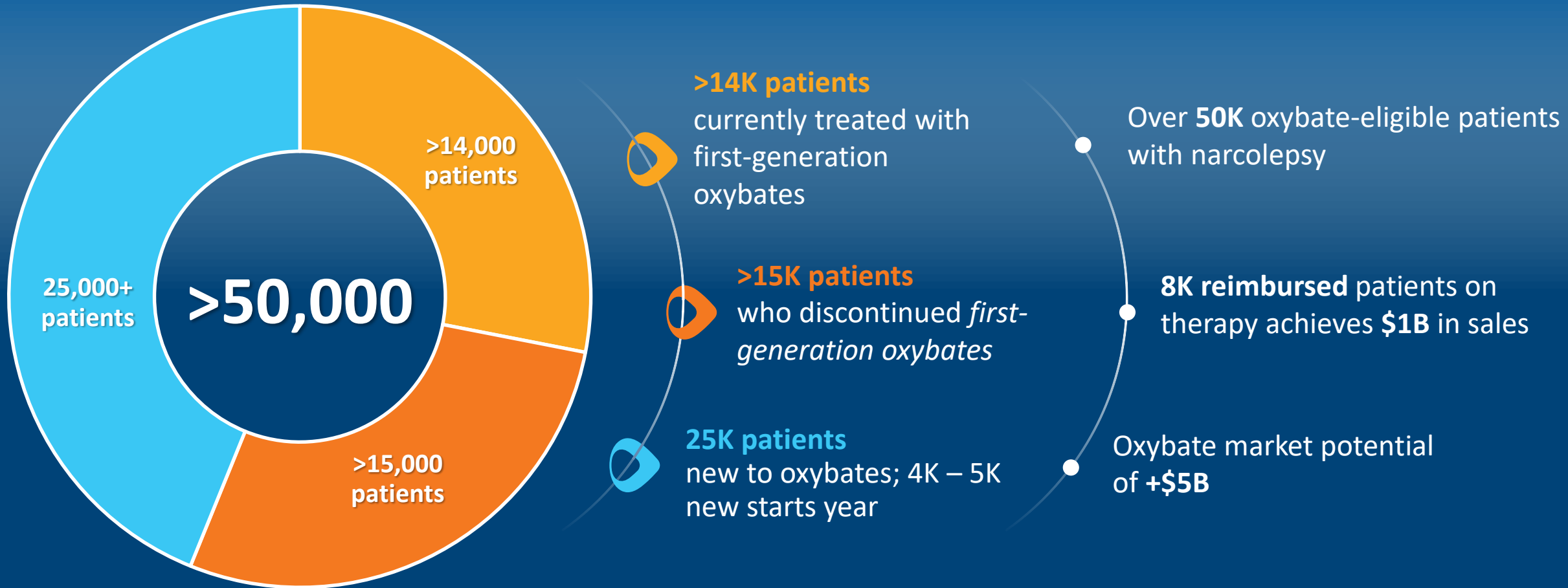
In narcolepsy, the body cannot separate wake and sleep – they blend together. Key symptoms include the following:

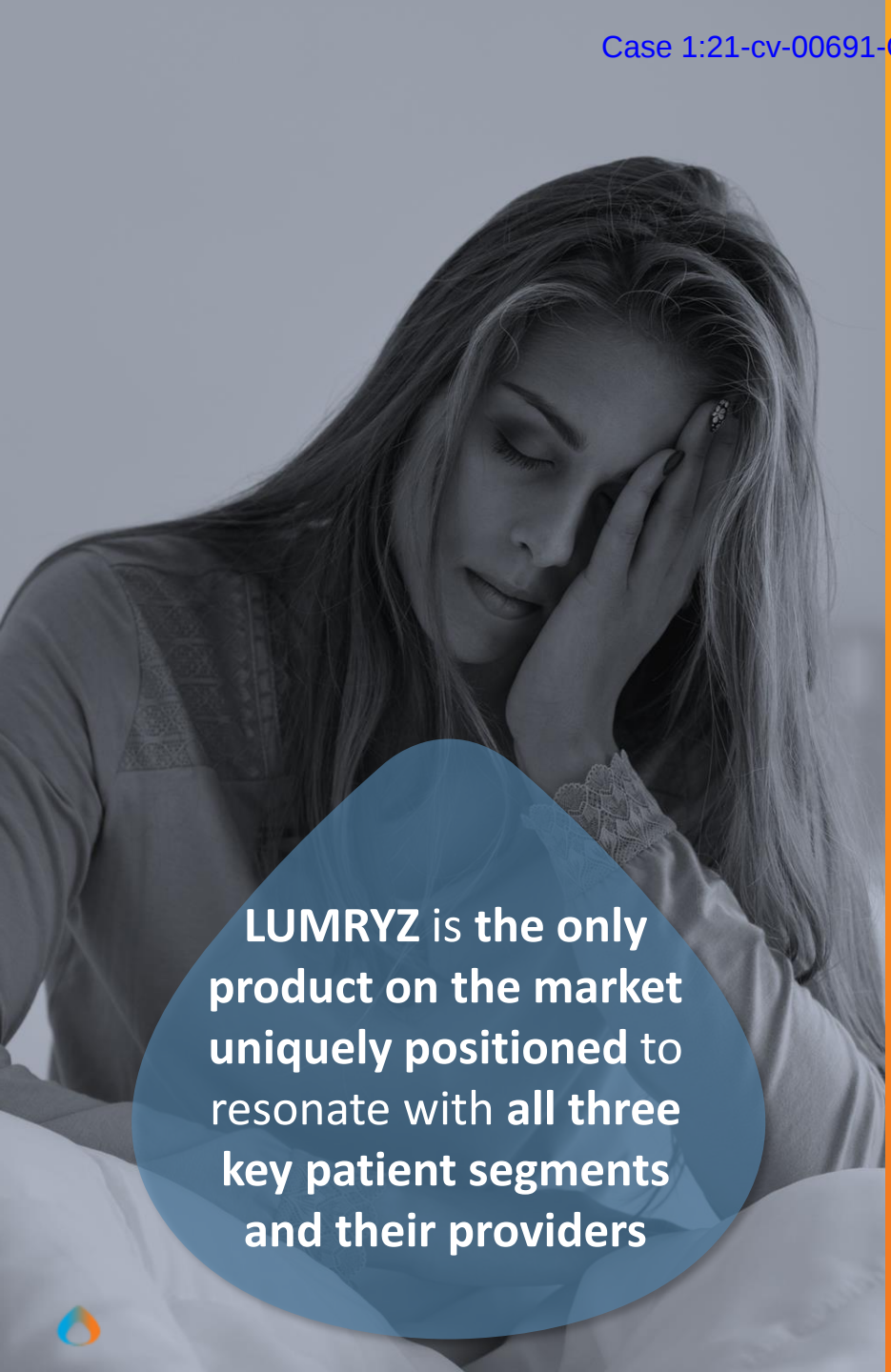
1. **Excessive daytime sleepiness (EDS)**, pathological sleepiness during the day.
2. **Cataplexy**, the sudden onset of weak or paralyzed muscles, usually brought on by strong emotions or certain situations.
3. **Disrupted nighttime sleep (DNS)**, or fragmented sleep, waking up multiple times a night for 10–20 minutes at a time.

Narcolepsy affects approximately 1 in every 2,000 people in the United States (0.02%-0.18% of the population)

Oxybates are the only class of drugs that addresses all 3 symptoms of narcolepsy

LUMRYZ Peak Sales Opportunity is >\$1B For Narcolepsy





LUMRYZ is the only product on the market uniquely positioned to resonate with all three key patient segments and their providers

~40%

Of eligible patients state middle-of-the-night dosing is one of the main reasons they have not tried a twice-nightly oxybate

>25,000

Eligible patients have never started an oxybate

>90%

Of providers who have never prescribed an oxybate agree that middle-of-the-night dosing is a challenge for patients that causes negative consequences

>200

Providers who had never previously prescribed an oxybate have written for LUMRYZ

~94%

Of patients who switched from first-generation oxybate prefer LUMRYZ dosing



Laser-Focused on the Levers That Propel LUMRYZ's \$1B Opportunity in Narcolepsy¹



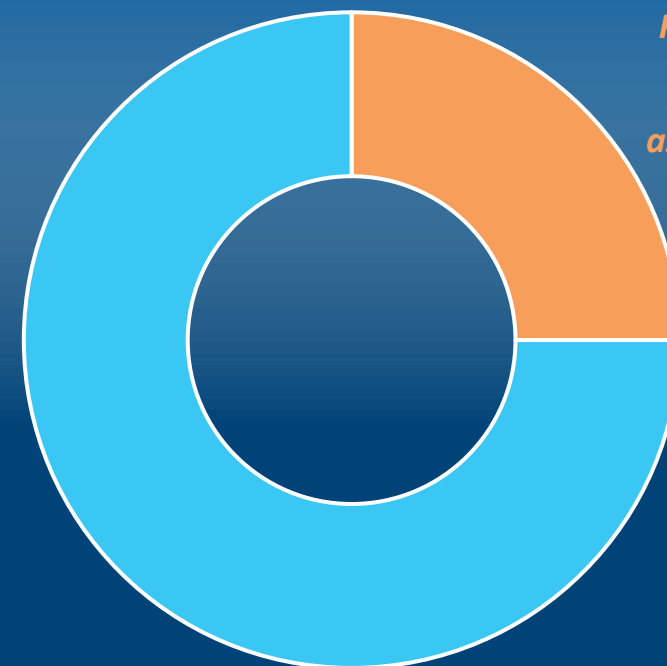
Accelerate our investments to drive demand from all patient types and further **unlock switch patient opportunity**



Drive improvements in persistency, especially with new to oxybate patients



Further our overall **physician reach and impact across** all patient segments



~8K Reimbursed Patients On Therapy Achieves \$1B in Sales²

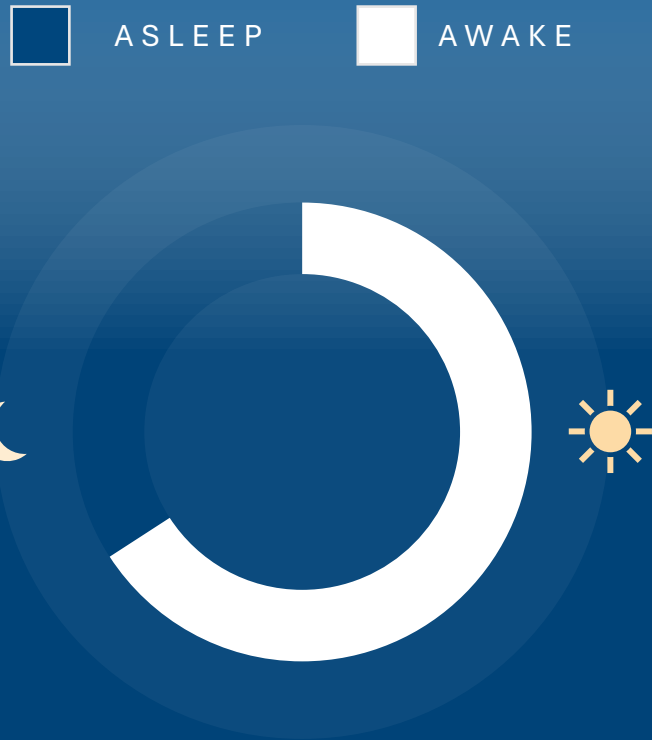
¹ Estimates based on current pricing and market dynamics

² Based on assumptions including assumed annual price increases, gross to net adjustments, persistency and compliance



~65% of Patients with Narcolepsy Experience Poor, Fragmented Sleep in Addition to their Daytime Symptoms, Despite Getting Adequate Rest

SLEEP CONSOLIDATION

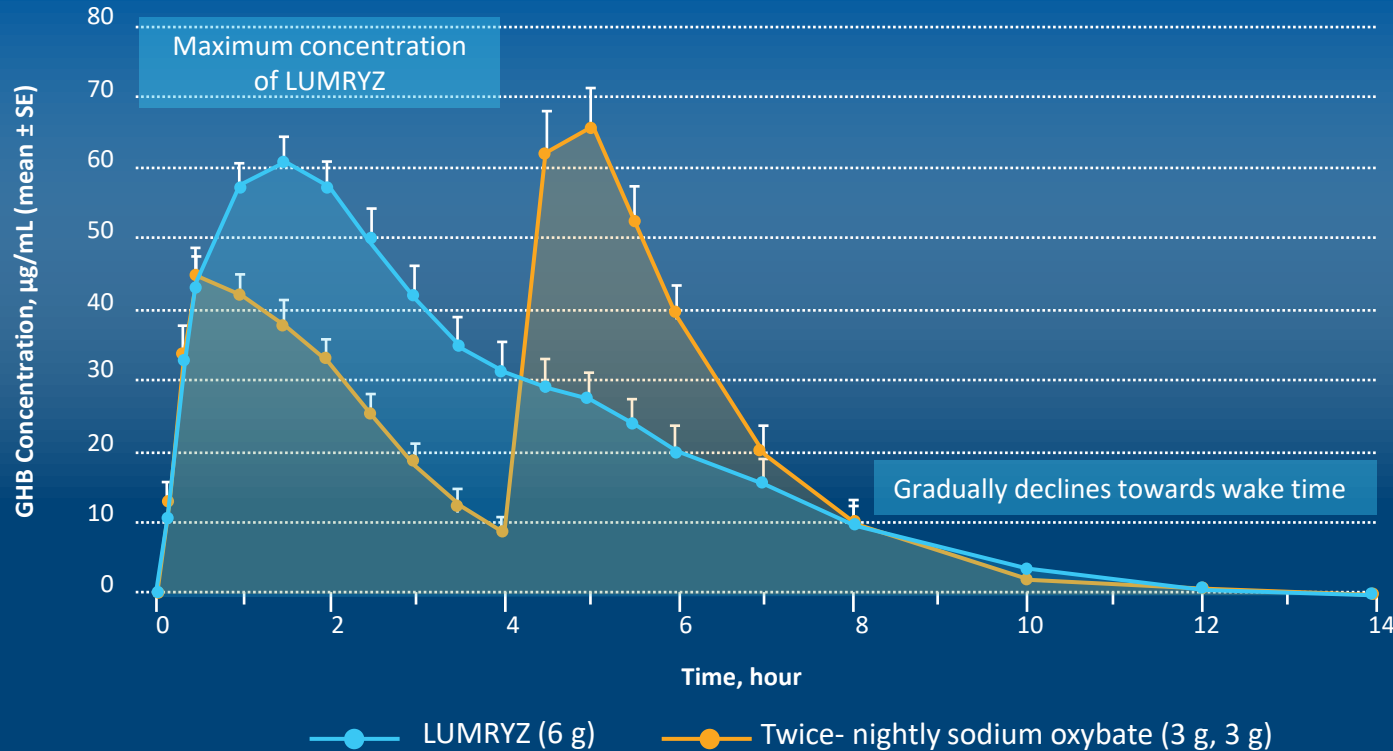


NORMAL



NARCOLEPSY

Once-Nightly Dosing is a Significant Differentiator Vs. First-Generation Oxybates



Granted Orphan Drug Exclusivity based on FDA's determination that once-at-bedtime LUMRYZ provides major **contribution to patient care** over first-generation oxybates, which require nocturnal arousal and increase disrupted and/or fragmented sleep

*The phase 1 study was designed to evaluate the relative bioavailability, safety, and tolerability of LUMRYZ compared to twice-nightly sodium oxybate.**

LUMRYZ concentration 8 hours after dosing fell below the bioequivalence criteria to twice-nightly sodium oxybate, providing reassurance of lack of residual morning grogginess.*

*Based on a determination of Orphan Drug Exclusivity by the FDA Office of Orphan Products Development (OOPD) between LUMRYZ and Xyrem or Xywav. There are no head-to-head data for LUMRYZ and Xyrem or Xywav.



Launch to Date¹

~\$250

Net revenue (\$M)

2,800

Patients on therapy

>2.5 : 1

LUMRYZ Net Patient
Adds vs Twice Nightly
Mixed-Salt Oxybates
Since July 2023

Since its launch in June
2023, LUMRYZ has seen
consistent patient uptake





2025 LUMRYZ Key Launch Priorities

>90% **Of Commercial Lives Covered;** *Contracts in Place with All Three PBM-Owned GPOs*

All patients have **access to patient support programs**, including...

Essential access and affordability programs

- ✓ \$0 commercial copay program
- ✓ Patient assistance program
- ✓ Temporary assistance program

Personalized support for patients and offices

- ✓ Nurse Care Navigators individually assigned to each patient & office
- ✓ Prior Authorization Certified Specialist

RYZUP
SUPPORT SERVICES

Healthcare provider support

- ✓ Team of Field Reimbursement Managers directly supporting offices
- ✓ Integrated data platform triggers to field teams and RYZUP team



Targeted initial launch strategy has resulted in meaningful penetration with early adopters

EARLY LAUNCH STRATEGY:
Targeted and focused

Early Adopters
(~25% of oxybate market)

Represent ~**60%** of total
LUMRYZ patient starts

2025 LAUNCH STRATEGY:
*Capitalize on momentum
with early adopters to
drive growth with
broader provider base*

**Remaining
Prescriber Base**
(~75% of oxybate market)

Represent ~**40%** of total
LUMRYZ patient starts

Note: Results are preliminary and based on data through 3/31/25.



Increasing Investments in Salesforce and Nursing Teams to Drive Patient Uptake and Market Expansion



Leverage LUMRYZ's value proposition to **grow switch and total patient uptake** with increased direct to physician and direct to oxybate patient investments



Achieve market leadership in the **new to brand (NBRx) patient segment** while capitalizing on the emerging market expansion



Increase **reimbursed patient mix to 80%** and beyond with account and channel specific strategies

Investments focused on higher-touch, more frequent, and more personal support services to better help patients transition and stay on LUMRYZ





Improving LUMRYZ Persistency Can Have an Increasingly Material Impact on Revenue as Total Patients on Therapy Grow



Doubling nursing team at our patient services center allowing for more frequent/tailored patient interventions



Increasing our field support team to **deliver physician-specific interventions** ahead of a patients' LUMRYZ refill



Expanding **partnerships with specialty pharmacies** deploying custom compliance and persistency programs



Investing in **field-based patient support services** for a more personal, high-touch intervention



LUMRYZ Expansion Opportunities

Idiopathic hypersomnia (IH) is a **rare sleep disorder characterized by excessive daytime sleepiness (EDS)** not attributable to any other medical conditions; **42,000 patients diagnosed with IH in US**

~10% treated
*with the only FDA
approved oxybate
treatment*

Initiated REVITALYZ™ Phase 3 trial to evaluate the efficacy and tolerability for LUMRYZ in IH; total target of ~150 patients participating for a 14-week period

Expected enrollment completion date – Q4 2025



Strong and Experienced Management Team and Board Of Directors with Proven Success Recognizing and Unlocking Value

Clinical



Delivered a once-nightly treatment option for patients with narcolepsy, a drug class that hasn't experienced significant medical innovation in over 20 years

Regulatory



Navigated two approval processes with Orphan Drug Exclusivity (ODE) for LUMRYZ in adults and children over 7 years of age; successfully designed two pivotal Phase 3 studies in alignment with FDA

Commercialization



Successfully built and scaled commercial organization for LUMRYZ in narcolepsy, which has generated strong and consistent demand with >2,800 patients on therapy*, outpacing twice nightly mixed-salts competitor ~2.6 : 1 since July 2023

Transformed the Company by **commercializing LUMRYZ**, a product with blockbuster potential changing the narcolepsy treatment landscape



A Leader in the Sleep Space With Substantial Growth Opportunities



Meeting Unmet Needs in Narcolepsy

94%¹ of patients prefer LUMRYZ over first-generation oxybates due to once at night dosing; awarded Orphan Drug Exclusivity for major contribution to patient care



Opportunity For Growth In Narcolepsy

\$5B future oxybate estimated market value represented by >50K patients; LUMRYZ represents a \$1B+ peak sales opportunity



LUMRYZ Beyond Narcolepsy

Ongoing Phase 3 REVITALYZ trial evaluating LUMRYZ for use in Idiopathic Hypersomnia, a disease with >40K patients diagnosed



Strong Financial Position and IP Protection

Existing capital + sales sufficient to support LUMRYZ launch; strong balance sheet with no debt; Multiple Orange Book-listed patents, 16+ years of Intellectual Property protection into 2042

Focused on transforming medicines to transform lives



¹Roy A, Harsh J, Akinyemi AO, et al. Patient Preference and Nocturnal Experience With Oxybate Treatment for Narcolepsy: Interim Analysis of Data From RESTORE. Chest 2022, Oct 16-19, 2022: Nashville, TN.



Financials

Financial Summary¹

(\$ in millions)	Q1	
	2024	2025
 Product Revenue	\$27.2	\$52.5
 Operating Expenses	\$51.7	\$49.9
 Operating Loss	(\$26.0)	(\$3.0)
 Cash, Cash Equivalents & Marketable Securities	\$88.8	\$66.5

1 – Refer to Forms 10-Q for the periods ended March 31, 2024 and 2025 for full financial results.



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40065

GAAP vs. Non-GAAP Reconciliation

(\$ in millions)	Q1	
	2024	2025
 GAAP Operating Loss	(\$26.0)	(\$3.0)
 <i>Stock Based Compensation</i>	\$5.4	\$4.2
 <i>Depreciation & Amortization ¹</i>	\$1.1	\$0.8
 <i>Transaction Costs ²</i>	\$0.5	\$ -
 Non-GAAP Operating (Loss) Income	(\$19.0)	\$2.0

1) Includes depreciation of fixed assets and amortization of prepaid expenses

2) Expenses incurred for the mandatory exchange of the Company's American Depositary Shares for the underlying ordinary shares and the termination of the American Depositary Receipt Program

3) Totals may not sum due to rounding



Revised 2025 Guidance

	<i><u>Current Guidance</u></i>	<i><u>Prior Guidance</u></i>
 Revenue	\$255 - \$265M	\$240 - \$260M
 Cash Operating Expenses	\$180 - \$200M	\$180 - \$200M
 Cash Flow	\$30 - \$40M	\$20 - \$40M
 Patients on Therapy at 12/31/2025	3.4 – 3.6K	3.3 – 3.5K



Join us on our
transformational journey



EXHIBIT 11

Business Update Call *(Corrected version)*

✓ **Event Details**

Date: 2025-01-08
Company: Avadel Pharmaceuticals Plc
Ticker: AVDL-US

✓ **Company Participants**

Austin Murtagh - Precision AQ, Director
Gregory J. Divis - Avadel Pharmaceuticals Plc, Chief Executive Officer & Director
Thomas S. McHugh - Avadel Pharmaceuticals Plc, Chief Financial Officer

✓ **Other Participants**

Francois Brisebois - Analyst
Andrew Tsai - Analyst
Marc Goodman - Analyst
Ami Fadia - Analyst
Oren G. Livnat - Analyst
Ashwani Verma - Analyst
Myriam Belghiti - Analyst
Chase Knickerbocker - Analyst

MANAGEMENT DISCUSSION SECTION

Operator

- 00:00:04
- Greetings and welcome to Avadel Pharmaceuticals Business Update Conference Call. At this time, all participants are in a listen-only mode. Accompanying slides for this call can be found on Avadel's Investor Relations website. A question-and-answer session will follow the formal presentation. As a reminder, this conference is being recorded.
- 00:00:26
- It is now my pleasure to introduce Austin Murtagh with Precision AQ. Thank you. You may begin.

Austin Murtagh

- 00:00:33
- Good afternoon and thank you for joining us on our conference call to discuss Avadel's business update and outlook for 2025. Moving to slide 2, as a reminder before we begin, the following presentation includes several matters that constitute forward-looking statements made pursuant to the Safe Harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements regarding the company's expectations on preliminary commercial metrics, unaudited financial results, forward-looking patient metrics, revenue opportunity and revenue estimates, and the success of the commercialization of LUMRYZ.
- 00:01:13
- Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those contemplated in such forward-looking statements. These risks and uncertainties are described in Avadel's public filings under the Exchange Act included in the Form 10-K for the year ended December 31, 2023, which was filed on February 29, 2024, and subsequent SEC filings. The forward-looking statements made today are as of the date of this call, and except

as required by law, Avadel undertakes no obligation to update or revise any forward-looking statements contained in this presentation to reflect new information, future events or otherwise.

00:01:54 In addition, we may refer to certain non-GAAP measures during this call, and these measures should not be considered in isolation or as alternatives to or substitutes for financial measures determined in accordance with generally accepted accounting principles in the United States.

00:02:11 On the call today are Greg Divis, Chief Executive Officer; and Tom McHugh, Chief Financial Officer.

00:02:17 At this time, I'll turn the call over to Greg.

Gregory J. Divis

00:02:21 Welcome, everyone, and thank you for joining us today. As we're now 18 months into the launch of LUMRYZ, we have decided to take a slightly different approach to our January business update and 2025 pre-announcement.

00:02:34 As such, turning to slide 3, today we will cover the following topics. We'll provide a LUMRYZ launch update and review priorities and actions being taken to accelerate the launch. We'll review our Q4 and full year 2024 preliminary results, and for the first time provide initial revenue guidance for 2025. We'll review the progress and the path forward toward achieving the \$1 billion potential revenue opportunity for LUMRYZ, and lastly provide an update on our lifecycle management programs and our 2025 key milestones.

00:03:07 Moving to the next slide, as a company, we've made tremendous progress over the last few years, building our business and capabilities to enable our transformation of the sleep space for patients, for their families, and their healthcare providers, while overcoming attempts by our competitor Jazz to delay LUMRYZ coming to market.

00:03:25 Our progress has been brought to life for me recently with a patient story from Texas. A nurse practitioner working in the emergency room was really struggling with the dosing of the first generation mixed-salt product, and as such, in discussion with her physician, made the decision to switch to LUMRYZ. And according to her sleep specialist, she is functioning better and has also been able to decrease her daily dose of stimulant. Most importantly, she has expressed how happy she is with her now simplified and effective treatment regimen.

00:03:57 This is just one of many examples of the feedback we regularly receive from physicians and patients alike. Based on this feedback, the impact we're having, and the progress made to-date, we remain confident in our belief that LUMRYZ is a best-in-class therapy for people with narcolepsy and is on its way to market leadership. Like other rare disease products at this early stage of launch, we are in a critical period of establishing the initial foundation upon which the continued and future success of LUMRYZ will be built.

00:04:27 On slide 5, as we move into 2025 and our foundation continues to strengthen, our LUMRYZ launch priorities are threefold: first, expanding our physician reach and impact across all patient segments; second, accelerating our investments in activating switch patients; and finally, driving improvements in patient persistency. 2025 will be a year of growth and a year where we can and will go further and faster. So, let's review our launch to date results and our key priorities for this year.

00:05:01

Moving to slide 6, since launch, we have delivered strong and consistent demand in our initial primary targeted audience, resulting in nearly \$200 million in net sales, more than 3,700 patient starts, and greater than 2,500 patients on therapy today. From a patient perspective, we have generated demand from all patient types, which was initially led by switch patients at approximately 50% of all patient starts.

- 00:05:28 More recently, on slide 7, we have seen a shift in our patient mix, with the rapid growth of new to oxybate patients, who, when combined with previously treated patients, in Q4, represented 62% of all starts. Importantly, reimbursed patients now represent nearly three-quarters of all patients on therapy.
- 00:05:50 As stated on slide 8, these results have been primarily driven by two physician segments. First, we have seen successful LUMRYZ uptake with a segment of physicians who have become our early adopters and are core to the foundation we are building. This group of less than 500 early adopters have delivered nearly two-thirds of all LUMRYZ patient starts, yet only represent a quarter of the total oxybate market opportunity. The second group of physicians are those who have previously never prescribed an oxybate before. This group now represent approximately 15% of our patient starts, further validating the emerging market expansion opportunity LUMRYZ offers.
- 00:06:31 These early successes are the result of focused commercial execution against important segments of prescribers, which validates that we can generate significant LUMRYZ demand. This also demonstrates that we have much more work to do in this highly competitive and concentrated rare disease market. With the same level of focus and consistent execution during 2025, we believe we will achieve significant results with the remaining 75% of the existing oxybate market we have not yet materially penetrated. This group of underpenetrated prescribers is a key pathway to continued growth, and in particular, switch patient growth, a primary focus for us in 2025.
- 00:07:15 Based on our ongoing physician and patient market research, which is supported by our promotional response analysis, these physicians are typically slower adopters and require more consistent and improved commercial execution and impact, which is something we have addressed. In addition, we are deploying programs and initiatives to unlock future switch patients. This is important, as some patients, based on research, can be concerned about reimbursement matters such as out-of-pocket costs or even losing access to oxybates if they consider switching, all of which are being actioned.
- 00:07:51 Turning to slide 9, switch patients are and will remain a critical focus, as they typically have an easier path to securing reimbursement and initiating LUMRYZ. They have proven to have meaningfully higher persistency rates, and on average represent a greater revenue opportunity.
- 00:08:07 As such, as stated on slide 10, our demand-based priorities for this year are focused on accelerating the growth of patients on therapy, and in particular switch and reimbursed patients. We will do this by expanding and upgrading our sales force and deploying tools and tactics to drive greater switch patient focus and impact on this underpenetrated market opportunity. We're increasing our direct-to-oxybate patient marketing efforts to accelerate oxybate patient education and activation to ask for LUMRYZ, while continuing our pursuit of market leadership in the new-to-brand oxybate patient segment and capitalizing on the market expansion momentum we are building. And lastly, we'll continue our focus on increasing our reimbursed patient mix toward 80% and beyond, with account and channel specific strategies. If patient demand is priority one, persistency improvements are a priority 1a.
- 00:09:01 Moving to slide 11, the narcolepsy market has had longstanding challenges with successfully keeping patients on oxybate therapy. First generation oxybates have historically experienced more

than 50% of new patients discontinuing therapy each year, with approximately half of that in the first 30 days.

- 00:09:22 More recently, based on data we have reviewed, the 12-month discontinuation rate for new first generation oxybate patients is now approximately 65%. This is something we believe hasn't received the attention it deserves, as there wasn't any competition, but now there is, and for us it is a priority. Just as we believe LUMRYZ will become the treatment of choice for oxybate eligible people with narcolepsy, we're equally committed to being the leader in persistency as well, helping ensure patients have their own personal optimal LUMRYZ treatment experience and the associated benefits they deserve.
- 00:09:56 For LUMRYZ, we expected persistency would be impacted, as our patient mix became more heavily weighted to new to oxybate patients, and our cumulative cohort of existing patients grew. This expectation has materialized, as our new to oxybate patient cohort is growing, which, from a persistency perspective, is being addressed with actions we believe will improve this important metric.
- 00:10:18 As it states on slide 12, specifically what we know is adverse events are one of the primary reasons for discontinuations. These tend to be common oxybate specific side effects such as nausea, dizziness, and vomiting that typically occur when starting or increasing a dose, and depending on severity, can lead to potential discontinuations. However, they generally subside within 1 to 2 weeks, providing an opportunity to impact this by ensuring expectations are appropriately set with patients, and deploying timely patient-specific interventions.
- 00:10:54 This is important because as patients progress through their steady-state dose and efficacy increases, satisfaction with their treatment increases and the likelihood of discontinuation declines, especially early in a patient's treatment, as nearly two-thirds of discontinuations occur in the first 90 days, thus providing a very clear window and opportunity to deploy patient-specific tailored messaging.
- 00:11:18 And even though LUMRYZ's persistency rates are higher than that of the first generation oxybates, that is neither good enough nor the appropriate standard. This year, we believe there is an opportunity to improve the overall persistency rate, which begins by impacting the first 90 days of treatment and stabilizing the overall discontinuation rate.
- 00:11:38 Transitioning to slide 13, to address this, we have recently made meaningful changes to both our strategy and our resources, including doubling our nursing team and our patient services center, allowing for more frequent and tailored patient interventions, including prior to the start of therapy, to better set treatment expectations. Increasing our field support team to deliver physician-specific interventions in advance of their patient's LUMRYZ refill, expanding our partnership with our specialty pharmacies, deploying custom pharmacy-based compliance and persistency programs, and lastly progressing additional field-based patient support services that can go beyond the traditional telephonic and digital intervention tools to a more direct, personal high-touch intervention at the patient and physician office level.
- 00:12:25 All these investments are designed with the goal of improving persistency, both early in and throughout a LUMRYZ patient's treatment experience, by delivering the right message to the right patient at the right time.
- 00:12:37 So wrapping up, we are committed to leading the way for patients in persistency and beyond, all the while providing the opportunity to free oxybate eligible people with narcolepsy from forcibly

waking up in the middle of the night, night after night, for a condition that is FDA stated is antithetical to the goal of improving sleep.

00:12:56 Now to translate this into our Q4 results and 2025 financial expectations, let me turn it over to Tom.

Thomas S. McHugh

00:13:02 Thanks, Greg. We'll start with how we currently estimate 2024 will wrap up, followed by our expectations for 2025 and beyond. Moving to slide 14, I'll highlight a few preliminary 2024 fourth quarter results and will provide more detail when we announce full year earnings later this quarter.

00:13:22 Starting with Q4, we estimate the net revenue will be approximately \$50 million, compared to \$19.5 million in the fourth quarter of 2023. We also estimate Q4 revenue was impacted by approximately \$6 million, as there was about 1.5 less weeks of inventory in the channel at the end of Q4 versus the end of Q3.

00:13:42 GAAP operating expenses are expected to come in at approximately \$50 million, and excluding about \$6 million of non-cash charges for stock-based compensation and depreciation and amortization, cash operating expenses are estimated at approximately \$44 million. Importantly, our cash flow metric continues to improve, and cash flow for the quarter was positive, and ending cash will be approximately \$73 million at December 31 versus \$66 million at September 30.

00:14:11 With respect to some key patient metrics, there were over 600 patient starts during the quarter, resulting in increase of over 200 patients on therapy. We saw a slowdown in conversion of enrollments (14:20) to patients starting therapy as we entered the holiday season. And absent the holiday impact, we believe that patient starts would have been consistent with the 700 per quarter pace of the first three quarters of the year. During 2024, there were more than 2,700 patient starts and over 3,700 since launch, and all of which resulted in 2,500 patients on therapy as of December 31, compared to 900 at the end of last year.

00:14:50 I'll turn now to slide 15 and current expectations for 2025. Earlier, Greg reviewed our key launch priorities, and depending on the execution against those, as well as other plans and assumptions, we are projecting the following full year results.

00:15:07 Revenue is projected to be in the range of \$240 million to \$260 million, which represents about a 50% increase at the midpoint of guidance over 2024 full year revenue. We believe that 2025 is forecasted with an appropriate degree of conservatism regarding patient starts and patient mix, which are weighted more heavily to new to oxybate patients, and revenue could be higher, with improvements in several key assumptions, such as patient demand, patient mix, and persistency.

00:15:37 And with a highly leverageable cost structure, we also expect the cash flow for 2025 will be positive, and in the range of \$20 million to \$40 million, that we can fund the ongoing launch in Phase 3 IH study from cash on hand and cash flow from operations.

00:15:56 I'll wrap up my commentary on slide 16 with what we believe and how we can achieve the \$1 billion plus revenue opportunity for LUMRYZ. We expect that over the next several years, LUMRYZ will become the leading oxybate therapy for the treatment of narcolepsy and that the oxybate market will continue to expand, just as we have seen since the launch of LUMRYZ. The path towards achieving \$1 billion of revenue is straightforward, requiring a constant base of

approximately 8,000 reimbursed patients. And 18 months into launch, we are nearly 25% of the way towards achieving that goal, with over 1,800 reimbursed patients on therapy.

00:16:35 And with three patient segments totaling over \$50,000 – 50,000 patients, there are multiple paths to getting the number of reimbursed patients needed to achieve \$1 billion of sales. However, for example, if only 30% of the 50,000 patients initiate treatment with LUMRYZ and factoring in persistency, LUMRYZ will become \$1 billion-plus product, all of which is being built on a highly leverageable operating structure poised for significant cash generation earnings. At current gross margins, projected GAAP operating expenses, and our existing tax and capital structure, we estimate that reaching \$1 billion of revenue will yield approximately \$6 of diluted earnings per share.

00:17:18 And with that, I'll turn the call back to Greg.

Gregory J. Divis

00:17:21 Thank you, Tom. Before we wrap up and open it to Q&A, let me provide a brief update on the work we're doing with our lifecycle management programs on slide 17. First and foremost, we have a sustainable, high-growth franchise in LUMRYZ that can drive significant long-term value with current patent protection to early 2042. And that value opportunity extends potentially beyond that of LUMRYZ in narcolepsy.

00:17:46 As previously stated, we are conducting our Phase 3 REVITALYZ trial in idiopathic hypersomnia, or IH, which is currently enrolling as planned and is expected to be completed in the second half of this year. Of note, we have a legal matter we must resolve around the potential NDA filing and approval of LUMRYZ in IH. Assuming we are successful in this regard, we currently expect to be able to file the NDA approximately six months post completion of our pivotal trial. We have become quite bullish on the potential prospects of LUMRYZ and IH, both because of what we've learned and what we hear directly from clinicians and leading key opinion leaders.

00:18:25 As stated on slide 18, there are approximately 42,000 diagnosed IH patients under the care of physicians, yet less than 8% are being treated with the only FDA approved treatment. What we hear from clinicians is that many patients, due to their deep sleep inertia associated with IH, cannot physically wake up in the middle of the night to take a second dose, and therefore are not able to benefit from a full therapeutic treatment. As such, we routinely hear that the LUMRYZ value proposition for patients is potentially even greater in IH than in narcolepsy.

00:19:00 In addition, our formulation scientists continue to work with our third party partners on developing a once-nightly low or no sodium oxybate formulation, having a target product profile bioequivalent to LUMRYZ. And if successful, we intend to pursue FDA approval for this product to treat both narcolepsy and IH.

00:19:17 Turning to slide 19, as we start the new year, key milestones for this year include: our quarterly financial and launch-related results include revenue, patient demand, patient mix, and net patients on therapy; the successful completion of our pivotal IH trial and progress toward NDA filing readiness; updates on our no/low sodium development programs, and of course, our continued progress in ongoing litigation matters as previously noted, including the November antitrust jury trial against Jazz, as well as the advancement of our recent patent infringement suits we filed against Jazz to protect our once-nightly oxybate innovation.

00:19:58 Moving to slide 20, in closing, we have built a strong demand-based foundation for LUMRYZ, which continues. We're investing in the areas to accelerate the launch and address the challenges in our

pursuit of the \$1 billion LUMRYZ potential. We're advancing our lifecycle management programs that offer, if successful, a significant expanded oxybate market opportunity for LUMRYZ, all of which is supported by robust intellectual property portfolio extending into early 2042, a portfolio we are continually expanding.

00:20:28 LUMRYZ represents a meaningful value-creating opportunity built on a highly leverageable cost structure, which should result in significant cash and EPS generation over the coming years and through its patent life. Furthermore, this cash generation foundation creates potential optionality to invest in the growth of Avadel and/or return capital to our shareholders.

00:20:49 In 2025, we look forward to many more stories like our ER nurse practitioner from Texas. We're optimistic for the future and look forward to providing additional commercial updates as appropriate. We thank you for your time today, and as always, for your support. We will now open the line for Q&A. Operator?

QUESTION AND ANSWER SECTION

Operator

00:21:14 Thank you so much. One moment for our first question. It comes from the line of Francois Brisebois with Oppenheimer. Please proceed.

Analyst: Francois Brisebois

00:21:25 **Question – Francois Brisebois:** Hey, guys. Thanks for the questions and the update. I just wanted to better understand a little bit, maybe, Tom, if you can go into – if we just kind of see the patients on therapy, and we see the sales, right, there's the net revenue per patient that you kind of look at, that comes in at a certain number. Can you help us understand why – how to think about that number going forward, does it change, and maybe the change from that number versus third quarter and where it came in? Because it does seem like your number of patient starts was almost in line. The holiday took it off, but 600 was a solid quarter. So just a little more on the net revenue per patient and how that can get better with reimbursement. Thank you.

00:22:09 **Answer – Thomas S. McHugh:** Sure. Thanks, Frank. And maybe a good starting point is the question you asked at the beginning, which is where patients were at 12/31. And as we're thinking about revenue heading into 2025, we have to make an assumption that a percentage of those patients will discontinue during the course of 2025, which, of course, impacts the exit run rate.

00:22:29 And then in terms of comparison of Q3 to Q4, we did have net patient adds, perhaps a driver which we anticipated was going to happen was the change in the inventory level in the channel, which impacted revenue by about \$6 million.

00:22:48 **Question – Francois Brisebois:** Okay, great. And is that \$6 million, on that note, is that – because we – the inventory play is something to be expected a little bit. Was this \$6 million more than expected, or was that kind of in line with what you guys expected?

00:23:01 **Answer – Thomas S. McHugh:** Sure, Frank. I think from my standpoint, it was in line with what I expected. We signaled this during the Q3 call that we expected to be fewer weeks of inventory in channel 12/31. And it's really a function of capacity constraints, the storage constraints in the specialty pharmacies, where they had indicated they were at capacity into Q3. So, I wouldn't take it

– certainly would not take it as an indication of any slowdown in demand. It's just the specialty pharmacies just couldn't carry any more than they could at September 30.

00:23:30 In a normalized range, I think two to four weeks is a normalized range to think about. It's tough for me to predict where we get into Q1 or subsequent quarters, but I would think about inventory at least in the channel in that range of two to four weeks.

00:23:44 **Question – Francois Brisebois:** Okay, great. And then just lastly, going forward, in terms of metrics to be expected for us to understand better the persistency and the new patients versus the switch patients, is this something that you'll get clarity on going forward just to see how these actions are going, or we don't know yet?

00:24:02 **Answer – Gregory J. Divis:** Yeah, Frank, the way we think about it going forward is patient demand in the form of patient starts, patient mix in terms of source of patient, and of course net patients on therapy, we think all of those metrics will provide the sort of clarity you're looking for.

00:24:20 **Question – Francois Brisebois:** Perfect. Thank you very much.

00:24:22 **Answer – Gregory J. Divis:** Thank you.

Operator

00:24:23 Thank you. Our next question comes from the line of Andrew Tsai with Jefferies. Please proceed.

Analyst:Andrew Tsai

00:24:33 **Question – Andrew Tsai:** Hey, thanks. Good afternoon. Thanks for taking my questions and thank you for sharing the progress and expectations. So, maybe the first question around the 2025 guidance on the patient numbers, if I take the midpoint of patients initiating therapy in 2025, I think that's – I'm assuming that's on top of the 3,700 you have today. And if that's the case, then taking that resulting number and then working out the math with the patients on LUMRYZ guidance that you have at the midpoint, basically is it correct to think that the implied discontinuation rate by year-end 2025 could be closer to 50, 5-0, percent? I'll start off with that. Thanks.

00:25:17 **Answer – Thomas S. McHugh:** Yeah. Hey, Tsai, listen, Andrew, I don't disagree with your math, so that is what it implies. This is one of those areas we think there's really great opportunity for improvement versus our current assumptions, which is why we've made the investments we've made around persistency and in driving patient demand. Because we believe we've taken appropriate approach towards forecasting 2025 at a conservative level, and what we are thinking about for 2025 is that we're going to be more heavily weighted towards new-to-oxybate patients, which does impact overall persistency.

00:25:52 **Question – Andrew Tsai:** Thanks. And I guess I'd have to think about it more, but you did mention how your current guidance is conservative, but makes me think how conservative is this. Ultimately, how much higher could these revenues be ultimately? Do you have actually a little bit more color around that? And then, how much is it from the – in terms of growing patient volume or driving less discontinuations more realistically that can drive higher sales in 2025?

00:26:29

Answer – Gregory J. Divis: Yeah, Andrew, I think first of all, I think most important is, if we think about the first six quarters of launch, we had a strong start. We clearly have hit some challenges with persistency here in the second part of 2024, and we have taken the actions to address those persistency matters and also ensure our focus on driving switch patients.

00:26:56 So your question as to which one is more important, the answer is they're both important. And I'll just, again, restate that if you look at where we've indexed our efforts early in the launch in our early adopters, we have actually significantly penetrated that audience. And it's over-representative of their potential within the oxybate market. If we can continue to replicate that over time, we should have that sort of success and beyond across all patient segments.

00:27:25 So, we do think there are opportunities to improve and beat, if you will, how we've guided. I would say at this point, we need to continue to assess the interventions and the impact of those interventions and give us opportunity in subsequent quarters to provide more clarity in that regard.

00:27:47 **Question – Andrew Tsai:** Thanks. And then very last quick question, maybe you did share in the slides and I missed it, how should we think about the overall mix of your LUMRYZ patients going forward by year-end? Would you still expect the same proportion that you're seeing right now, year-end 2024? Thanks.

00:28:06 **Answer – Thomas S. McHugh:** Yeah. So, Andrew, it's Tom. So what we had put on the slides, the mix of patients in the fourth quarter was certainly more heavily weighted towards new to oxybate and previously tried and discontinued. As we're looking into 2025, and again, I would view this as one of those assumptions we made on more conservative basis, we think we're going to continue to be overweighted in terms of new to oxybate and previously tried and discontinued, and improving the patient mix will certainly drive an improvement in revenue.

00:28:37 **Question – Andrew Tsai:** Thank you so much.

Operator

00:28:40 Thank you. One moment for our next question. That comes from the line of Marc Goodman with Leerink. Please proceed.

Analyst: Marc Goodman

00:28:48 **Question – Marc Goodman:** Yeah, a couple things. First, I may have missed this, but the average selling price was what? Like if it was \$100,000 in the second quarter and \$96,000 in third quarter, what was it in the fourth quarter?

00:28:59 **Answer – Thomas S. McHugh:** Hey, Marc, it's Tom. So, listen, preliminarily, of course, we're still closing the books, but it averaged about \$96,000 if you just take the revenue we reported and adjust it for the inventory of \$6 million, divide that by the average number of patients on therapy, works out to about \$96,000 for the quarter.

00:29:15 **Question – Marc Goodman:** So apples to apples, it's about – so it's the same as third quarter (29:20)?

00:29:20 **Answer – Thomas S. McHugh:** Subsequent with third quarter (29:21). That's right.

00:29:22 **Question – Marc Goodman:** Okay. Fine. And then just secondly, historically, when – I mean, in order to get to \$1 billion, are you basically counting on the IH indication? Is that we're counting on? I mean, when a product goes to 170 to 250 (29:37), I mean, obviously, a new indication can change the growth trajectory. But outside of that, we're used to seeing growth rates that kind of slow each after year. So, we have to be thinking that this indication slows a little bit over the next couple years in growth rates. It's not going to become \$1 billion in narcolepsy, right? This is narcolepsy and IH.

00:29:58 **Answer – Thomas S. McHugh:** Marc, the way we think about it, what we've talked about in terms of \$1 billion opportunity excludes IH.

00:30:06 **Question – Marc Goodman:** So, can you talk about is there an expectation that 2025 is a growth year of 40-something percent, whatever the number is, to get to the midpoint, and then it actually is faster in 2026? I mean, because traditionally, that's not normally what we see.

00:30:25 **Answer – Gregory J. Divis:** Yeah. I think from our perspective is there is a significant amount of patient opportunity to grow LUMRYZ, whether from the three different patient segments that Tom described, and our penetration of those respective patient segments doesn't have to be significant to be able to realize those sorts of numbers only in narcolepsy alone. And we've seen those levels of penetration in our early adopter audiences already, right.

00:30:51 So, if we can continue to translate that into the broader audience, then we believe over time, and the slope of that curve will progress the way it progresses, we can get to those sorts of numbers on patients, given the opportunity and what we hear in our market research, right, from that perspective.

00:31:09 I will say it's not a – it certainly is a therapeutic category where consistent growth continuously quarter after quarter after quarter has been demonstrated, and we believe we can continue to execute and deliver on that. We're not (31:22), and based on the patient source and opportunity we have and what we hear from our research.

00:31:32 **Question – Marc Goodman:** And just last question, because I guess this kind of answers when peak sales would be, peak sales would be in the year before you go LOE, when are you assuming the LOE?

00:31:43 **Answer – Gregory J. Divis:** Yeah, we're not defining when peak sales are. But at this point, as we described in the call, we have patent protection right now through early 2042.

00:31:54 **Question – Marc Goodman:** Thank you.

Operator

00:31:56 Thank you. One moment for our next question, please. Comes from the line of Ami Fadia with Needham & Company. Please proceed.

Analyst:Ami Fadia

- 00:32:08 **Question – Ami Fadia:** Hi. Good afternoon. Thanks for taking my question. Can you talk a little bit about what has been the dynamic with switch patients, and why we've seen a reduced mix of switch patients, and what your assumption is in your 2025 outlook for what percent of patients will be switch patients, and what do you think you need to do to really increase that mix? That's my first question.
- 00:32:33 **Answer – Gregory J. Divis:** Yeah. Again, I think the data shows what the curve we've seen early in the launch, a much higher percentage of them. And as we've gotten into the last couple quarters, it has slowed down and stabilized to a certain extent in the kind of low to mid – the mid, higher 30% of the total patient population – of our total patient starts.
- 00:32:55 In part, we've gotten, I would say, for lack of a better word, those who are waiting and looking for LUMRYZ. And now we're in – and in particular in our early adopters, and now we are in the market really expanding our reach and investing our efforts to both educate direct to patients through our direct to patient activities, to educate them and activate them to go seek LUMRYZ, where we've done that to date, we've seen that be successful. And we've expanded our sales force to expand our reach to be able to get wider and get more frequency into this other 75% of the underpenetrated market opportunity.
- 00:33:37 And we think in both those scenarios, we're going to continue to see growth in new to oxybate and previously treated and discontinued. And we're focused on accelerating the switch, which, if we do those things, our entire demand will grow.
- 00:34:00 **Question – Ami Fadia:** Got it. Just with regards to your guidance for 2025, you've sort of characterized it as something that has upside. What do you think could be the biggest driver of upside? And when you talk about the persistency rates of 50% that you've assumed in your guidance, what do you believe you need to do to sort of increase that persistency rate? And what could drive the persistency rates to be better than the Jazz products that have been on the market for many years? And then I have one quick last question.
- 00:34:39 **Answer – Thomas S. McHugh:** Sure. Hey, Ami, it's Tom. I'll take the first part of the question. There is – I would consider there's really three primary assumptions to drive revenue above the guidance we provided, each one of which is not insignificant and taken in combination, working together provides even more – larger results.
- 00:34:59 The three assumptions really are just really total patient demand, and of course, to drive more patients to the top and you have more net patient adds during the course of the year. Patient mix defined really is the mix of switch patients versus non-switch patients to characterize it simply. That's also a powerful driver of revenue. The higher the mix goes towards switch, the more revenue we believe we generate. And the third is persistency, which we're – believe we're making the right investments to improve that. And when you think of those three either individually or in combination, and that clearly would drive us above the (35:37) revenue guidance.
- 00:35:40 **Answer – Gregory J. Divis:** Yeah. And to your question of why do we think we can improve persistency vis-a-vis other products in the category, we've already demonstrated that we have higher persistency rates from the data we look at across all patient types at all time periods to date that we've been on the market. So we have numerically a better persistency rate, if you will. But from our perspective, as our patient mix shifted and the opportunity to keep patients on therapy, it's an investment and a priority for us, because we worked so hard to get them on therapy, and we know that when they get through the first 90 days, which is where the majority of the discontinuations occur, that their treatment experience and their satisfaction only continues to rise.

- 00:36:30 So, what we're really deploying is incremental resources deployed in particular centered around the first 90 days, where we engage with the patients, we engage with the office staff and physicians in an attempt to really positively impact from – before they start therapy to at different points in time during their journey, especially in the first 90 days.
- 00:36:52 Now every patient is important and every patient type is important in that regard, whether it's the first 90 days or beyond. And all of our programs are designed to impact everybody in that regard. But the new to oxybate and the previously treated and discontinued have markedly higher discontinuation rates than the switch patient, which is why the switch – why the mix of patient matters in that regard, why a focus on switch patients is important as well. But also, we have to have the tools and the tactics to try to meet the patient where they are and help them stay on therapy, which is something we haven't done until recently.
- 00:37:34 **Question – Ami Fadia:** Understood. Okay. Just last quick question, just could you elaborate on where the appeal to the injunction on IH is at, and what stage of the litigation we are at and when we can expect a decision?
- 00:37:51 **Answer – Gregory J. Divis:** All of what I can say on the appeal, the IH appeal, is that the oral arguments, I believe, are scheduled for February 7. And then we would – subsequent to that, we would expect a decision sometime from the appellate court sometime thereafter, right. When that is, not really sure, the last time we were in front of that group. On the REMS related patents, we had a decision in fairly short order, but it could also be later in Q1 or early in Q2, we don't know. So – but the oral arguments are February 7.
- 00:38:27 **Question – Ami Fadia:** Thank you.
- Operator**
- 00:38:27 Thank you. One moment for our next question. That comes from the line of Olive (sic) [Oren] (38:37) – one moment, please, from H.C. Wainwright, but I cannot read the name. Go ahead.
- 00:38:46 **Answer – Gregory J. Divis:** Hi, Oren.
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- Analyst:**Oren G. Livnat
- 00:38:47 **Question – Oren G. Livnat:** Hey, thanks. It's Oren. Can you hear me?
- 00:38:53 **Answer – Gregory J. Divis:** Yes.
- 00:38:54 **Question – Oren G. Livnat:** Great. Can you just talk a little bit more, and I'm sorry I had to jump on and off this call, so I'm sorry if you addressed it, but can you talk more about these interventions? I think you said they are sort of beyond traditional telephonic and digital interventions presumably. I don't know if that's mostly on the post-initiation patient support side, or if this is on the free initiation education side with doctors and/or patients. Just talk more about what are you doing differently that you didn't do before and why that wouldn't have occurred to you to do initially.
- 00:39:32 And also, maybe I missed this as well, but is the mix of patients that you're at now at this stage in the launch meaningfully different than you would have expected? And why do you think that is in terms of higher weighting towards new to patients? Is switching existing patients that weren't

already warehoused and eager and unhappy and waiting to switch to something, is that proving harder than you expected? Are patients just seeing their doctors less often than you expected, if you could just talk more about all of that? Thanks.

- 00:40:06 **Answer – Gregory J. Divis:** Yeah, Oren, in terms of the initiatives that we're taking on relative to persistency, whether it's the expansion of our nurses, whether it's the expansion of our field sales team, whether it's our partnerships with our specialty pharmacies or the additional field-based opportunities that we're evaluating and progressing, I would say all of them are things we hadn't been doing until recently. So, we continue to advance those capabilities from that perspective and assess their impact and how they are effectively improving the patients' treatment experience.
- 00:40:47 So, I think the one thing we've learned over the course of – in particular the last number of months is that the notion of one size fits all isn't the right approach, right? Each patient type has their own different nuance, and how we intervene based upon the patient is really, really important, and we continue to get smarter as we talk to patients about that and how we can become more, if you will, almost predictive in terms of who's at risk of a discontinuation and how do we deploy interventions in advance of that to prevent it, right, from that standpoint.
- 00:41:20 So, in terms of your comment about – your question about switch patients, I think the first thing I would comment is that the switch opportunity is robust for us, and it hasn't changed and we think it still represents respectfully the largest portion of our patient starts, right? It's rep, and I think that is in part because of the – some of the low-hanging fruit we got. And I think we're now in a rare disease where we are unlocking patients. We are in offices and online communicating to patients and physicians to give them the reasons why they should or – should consider LUMRYZ.
- 00:42:04 And we've done a lot of research in this regard, and we noted some of that research. Some of their concerns or hesitation is centered around reimbursement or concerns about out-of-pocket costs, which certainly isn't an issue for us, but certainly is something that we've got to make sure patients understand as one example of the things that they're comfortable with as they consider changing a therapy in a rare disease where only a handful of – a small subset of physicians have a lot of patients, most have a few patients, and the intervention opportunities aren't regular like our larger mass markets.
- 00:42:45 **Question – Oren G. Livnat:** Okay. And there's a lot of moving parts in this guidance, and I will admit it's a bit confusing at least from – without having a chance, more time to dig into it here. But just as we think about size of the (42:57) math of just discontinuation rates, which will hopefully improve on average, is there any sort of phasing or cadence that you expect in this year with regards to some of these new – all of the above new starts and different patient types coming online with these initiatives? Is this going to be a back-half weighted – I guess it speaks to Marc's question earlier that will be – come out of the year maybe at a higher growth rate than we are in the first half as these initiatives take hold?
- 00:43:33 **Answer – Gregory J. Divis:** Yeah, Oren, maybe I'll start, and then maybe Tom can wrap a little bit additional commentary. I think first, the thing that's very clear to us, and even was clear during the first four, five quarters of launch, where we were building this really strong foundation, is that the demand at the top of the funnel. Whether you measure that in enrollments or new patient starts continues to be robust and strong and consistent and we see that not changing. The opportunity for that to accelerate is really continuing the growth we're seeing in new-to-oxybate and switch patients, but add in a growth – if you will, an improvement in switch patients, right, from that perspective. So, that's why it's a focus for us.
- 00:44:16 How long it takes for these investments to take hold and have consistent impact is something we're evaluating all the time. I certainly believe that we've got our field teams and our nurses

team, nursing teams and whatnot all in place now and trained and operational here as we enter the new year. And we'll continue the effectiveness of those initiatives to be able to both build demand, like we think we can, and keep patients on therapy like we think we can.

00:44:52 **Question – Oren G. Livnat:** And just lastly, I'm sorry, did you say how many reps you had and now have in the field?

00:44:58 **Answer – Gregory J. Divis:** We've added about 15% on the rep side. We've doubled our field support teams, and we've doubled our nurses.

00:45:08 **Question – Oren G. Livnat:** Okay. How many reps is that out there now?

Answer – Gregory J. Divis: 53.

00:45:16 **Question – Oren G. Livnat:** Got it. All right. Thanks so much.

00:45:20 **Answer – Gregory J. Divis:** Thanks, Oren.

Operator

00:45:20 Thank you. One moment for our next question. And it comes from the line of David Amsellem with Piper Sandler. Please proceed.

Unidentified speaker

00:45:30 **Question – Unidentified speaker:** Hi. Thank you for taking our question. This is Alex (45:33) on for David. I've got one question for you. Looking ahead at longer-term dynamics, how are you thinking about adoption in IH for LUMRYZ assuming positive data? In other words, are you envisioning expanding the market, or do you see a lot of the LUMRYZ potential here coming at the expense of XYWAV? Just sort of help us understand how you're thinking about this opportunity.

00:45:57 **Answer – Gregory J. Divis:** Yeah. Again, I think, without providing a whole lot of commentary around this, given we've got to get through our clinical trial, get through our approval and here with the upcoming oral arguments and appeal process, I would say most importantly, and again, the research we've heard most recently and trying to understand the opportunity for LUMRYZ, is that there's a whole lot of room here for LUMRYZ to fit in, whether that – and I think the dynamics that we see in narcolepsy, to some extent, although there's more patients being treated in narcolepsy, we think, will likely potentially translate into IH to a certain extent. But the IH penetration today is, again, less than 8% based upon diagnosed patients and what we think are the actual IH patients on therapy with the twice nightly product.

00:46:49 So, from our viewpoint, there's a lot of room both inside of those being treated, but even bigger outside of that. And all indications we have, it's an opportunity to source all – from multiple patient segments, just like we've seen in narcolepsy accordingly, should we be successful in our clinical program and the related legal matters.

Unidentified speaker

00:47:14 **Question – Unidentified speaker:** Thank you.

Operator

00:47:14 Thank you. One moment for our next question, please. And it's from the line of Ash Verma with UBS. Please proceed.

Analyst:Ashwani Verma

00:47:27 **Question – Ashwani Verma:** Hi. Yeah, thanks for taking my questions. I have two. So, just for 2025, like I've been trying to do this math, but like what are you assuming on pricing? It seems like there is some disconnect even after factoring your 50% persistence. And I think that typically in this market, pricing doesn't necessarily get impacted that meaningfully. So that's the first one. And then second, has the recent leadership departure resulted in any kind of disruption in the sales momentum? Thanks.

00:48:03 **Answer – Gregory J. Divis:** So I'll take the second question. And from my perspective, the answer to that is no. In terms of disruption from the field, the field is very focused on what they're doing, and all of our field leadership team and our commercial leadership team is intact, still operating and driving the things that need to be driven from that perspective. So, in that point, we don't believe so, from what we've experienced so far. And on the pricing, I'll turn it over to Tom.

00:48:32 **Answer – Thomas S. McHugh:** Yeah, Ash, the way I would think about pricing is for a – listen, for a reimbursed patient who's on for full year, there's really no much of a change year-over-year from 2024 to 2025. But what does impact that when you get down to an average per patient number on an annual revenue basis is really the patient mix. And persistency does impact the calculation of the net revenue for switch patients versus the new to oxybate patient. And while we believe we've forecasted conservatively that factor, that mix of patients, does impact net revenue per patient on an overall basis.

00:49:16 **Question – Ashwani Verma:** Got it. Thank you.

Operator

00:49:16 Thank you so much. One moment for our next question, please. And it's from the line of Myriam Belghiti with LifeSci Capital.

Analyst:Myriam Belghiti

00:49:30 **Question – Myriam Belghiti:** Thank you for the update. Just one question for me, I'm just curious whether the factors driving discontinuation in the new to oxybate for LUMRYZ differ from those seen in the first generation oxybate. You mentioned that historically, those have been quite high. So, just wondering what gives you the confidence that these new initiatives will meaningfully address this issue.

00:49:52 **Answer – Gregory J. Divis:** Well, it's a great question, Myriam. And I think ultimately, as we've studied this and seek to understand what's happening and why, there's a few things that really stand out, right, is, number one, as we stated, across all time points and different patient segments, I would say that we numerically have better – or better discontinuation rates or we like

to think higher persistency rates, but not good enough, especially as our patient mix changes, and we are on a total patient population that's smaller, right, with 2,500 patients on therapy.

00:50:32 So for us, as we research this, talk to patients, talk to those who have experienced the sorts of things that drive discontinuations, it's clear that the majority of it happens early on. A big driver of that is how their expectations are set and how care is offered to them through the course of dose titration, because side effects come with starting and dose titration, yet they do subside over time, and – while your dose increasing to your steady state dose to get the ideal therapeutic effect, you're going to have adverse events along the way, and helping the patient navigate through those is really, really important.

00:51:10 So, again, our view is that we can have an impact in this regard. We have made the investments to do that, and we continue to deploy those efforts. And we'll have an opportunity to understand over time which ones we think are working the most effectively and how do we double down on those and which ones need to be enhanced and how do we do that.

00:51:34 **Question – Myriam Belghiti:** Got it. Thank you for answering my questions.

Operator

00:51:38 Thank you. One moment for our next question. It comes from the line of Chase Knickerbocker with Craig-Hallum. Please proceed.

Analyst:Chase Knickerbocker

00:51:50 **Question – Chase Knickerbocker:** Thanks and good afternoon. So just want to dig a little bit more on the efforts on the demand side and how you can improve the mix on what is entering the funnel and kind of maximizing switch patients. Can you just add a little bit more detail on how you're kind of focusing reps to kind of improve that mix entering the funnel more towards switch patients? Is there a decent number of kind of medium to high prescribers out there that are still kind of new to you and you still need to reach? Or is it mainly existing writers who have a meaningful cohort of oxybate users who are just sticking with first generation therapy? Thanks.

00:52:29 **Answer – Gregory J. Divis:** Yeah, I would – thanks, Chase. I would answer it this way, right. I think number one is you got to understand where the physician is on their buying – kind of in their buying journey, so to speak, and their adoption journey of LUMRYZ, right. In some case, we have physicians who have not prescribed. We have some high-volume prescriptions – physicians who have not prescribed. But by and large, our 25% of the market that's driving two-thirds of our volume to date, where we have really high penetration relative speaking, it's been directly related to our efforts and our promotion, right.

00:53:10 So I would say as you get to the other 75%, who may be slower adopters, may be harder to see, may be lower-tiered physicians who have fewer patients and some have a lot of patients, it really requires consistent – in our view, consistent focus and commercial execution against it. Understanding where that physician is in their kind of adoption sequence, is this a physician who we should be targeting the switch patient to? Is this one who we should be starting a new to oxybate with? Our focus though is to grow all patient demand with an emphasis on how do we unlock more switch patients, right.

00:53:46 And again, we are working with our teams to deploy those tools and tactics to do that. But there's ample opportunity across all of our segments, recognizing that where we've over-indexed our

time, we've done quite well, and that's laid the foundation. And now, we've got to expand that if we want to keep building and growing. And all of our research would tell us that that can happen. And that's what we're doing.

00:54:11 **Question – Chase Knickerbocker:** And then just last for me on the persistency side, is there any kind of early signs of success with any maybe earlier stage pilot programs that you've kind of put in place or specific teams out there in the field, in specific geographies who have done better from a persistency rate perspective? And kind of that you can share as far as potentially showing early signs of success at some of these efforts that you're instituting? Thank you.

00:54:35 **Answer – Gregory J. Divis:** Yeah, thanks, Chase. Given most of our resources are just operational now, I would say it's a little bit premature to draw any sort of definitive conclusions. I would say that what we've really tried to understand, in addition to what's happening at the physician, at the patient level, is to really understand where discontinuations are an issue at the physician level, right, in terms of perhaps their practice and how they manage patients, or what is the result – what is the resulting risk of discontinuation inside of specific physician practices. And taking the opportunity to engage and connect with those physicians who are doing a really, really good job from them, from their perspective, and from what the data tells us, learning and deploying and the sorts of lessons that they deploy, both not only at the patient level, but to the physician level as well. And that's the reason why we've expanded our resources to be able to do both.

00:55:39 **Question – Chase Knickerbocker:** Thanks, Greg.

Operator

00:55:40 Thank you. One moment, we have a follow-up from Marc Goodman with Leerink. Please proceed.

Analyst:Marc Goodman

00:55:48 **Question – Marc Goodman:** Yeah. Hey, just to follow up, since we're kind of resetting expectations here, Tom, first quarters are always a little funky. Maybe you can comment on first quarter a little bit and how to think about it. And then, second of all, did I see the numbers correct? You ended 2024 with 2,500 patients. You're expecting to end 3,400 patients at the end of this year. So like, if you just took like a simple average times the price, that's the same price as 2024, you get a number that's much above your range. So, what am I doing wrong?

00:56:28 **Answer – Thomas S. McHugh:** Let me break it down one by one. Literally the comment on Q1, Marc, we'll probably be in a better position to provide an update on that and how we're progressing when we do our Q4 call later this month or later this quarter. In terms of the effect on revenue for the year, you have to take 2,500 as we exited therapy, we're projecting that out of 800 to 1,000 patients that probably gets you to 3,300 to 3,500. And then I would, for simple math, take the average net revenue per patient we've been doing.

00:57:06 But don't forget, listen, you have to adjust the 2,500 starting point a little bit because of discontinuations. You don't get the full year benefit of those patients being on therapy.

00:57:18 **Question – Marc Goodman:** I see. So it's kind of a tight attrition issue. Okay. All right.

00:57:34 **Answer – Gregory J. Divis:** Thanks, Marc.

Operator

00:57:35 Thank you. And this ends our Q&A session for today. I will turn it back to Greg for final comments.

00:57:40 Thank you. Just a few final comments to say, first, thank you for spending your time and here on this afternoon, we look forward to any follow-ups. And again, after the first number of quarters of launch building our foundation, we do believe we are focused on the right things to both accelerate the demand and impact the persistency. And we look forward to providing those updates to you as we go forward. Thanks.

Operator

And with that, ladies and gentlemen, we conclude today's conference. Thank you for participating and you may now disconnect.

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EXHIBITS 12-14
REDACTED IN THEIR
ENTIRETY

EXHIBIT 15



NDA 212690/S-006
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SUPPLEMENT APPROVAL

Jazz Pharmaceuticals Ireland Limited
Attention: Arthur Merlin d'Estreux, M.Sc.
Director, Global Regulatory Lead – Neurosciences
One Commerce Square
2005 Market Street
Philadelphia, PA 19103

Dear Mr. d'Estreux:

Please refer to your supplemental new drug applications (sNDAs) dated February 12, 2021, received February 12, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for XYWAV™ (calcium, magnesium, potassium, and sodium oxybates) oral solution and NDA 21196 Xyrem (sodium oxybate) oral solution.

We acknowledge receipt of your risk evaluation and mitigation strategy (REMS) assessment dated February 26, 2021.

The Prior Approval supplemental new drug application 212690/S-006 provides for the new indication of Idiopathic Hypersomnia (IH) for XYWAV. NDA 212690/S-006 and NDA 021196/S-036 provide for modifications to the approved XYWAV and XYREM risk evaluation and mitigation strategy (REMS) to align with the revisions to the XYWAV prescribing information.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA (NDA 212690), including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for XYREM was originally approved on February 27, 2015, and the REMS for XYWAV was approved on July 21, 2020. The two drugs are subject to the same REMS, known as the XYWAV and XYREM REMS. The most recent REMS modification was approved on February 11, 2021. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of:

- Changes to the REMS materials to align with the new indication of Idiopathic Hypersomnia for XYWAV
- Changes to the REMS assessment timetable

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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- Change of the reporting interval for the Knowledge, Attitude, and Behavior Surveys from annually to every other year.

In accordance with section 505-1 of the FDCA, we have determined that the following REMS modifications are necessary to ensure the benefits of the drug outweigh the risks:

- Changes to the ***Patient Counseling Checklist*** to capture additional information regarding concomitant medication and alcohol use.

Your proposed modified REMS, submitted on February 12, 2021, amended and appended to this letter, is approved.

The timetable for submission of assessments of the REMS has been revised. Jazz Pharmaceuticals must submit a REMS Assessment on April 26, 2022, and annually thereafter.

The revised REMS assessment plan must include, but is not limited to, the following:

Program Implementation and Operations

1. REMS Enrollment Statistics (per reporting period and cumulatively)
 - a. Patients:
 - i. Number and percentage of newly enrolled patients stratified by age, geographic region (defined by US Census), indication, and gender
 - ii. Number and percentage of active patients enrolled (patients who received at least one shipment of XYWAV or XYREM during the reporting period) stratified by age, geographic region (defined by US Census), and gender
 - iii. Number and percentage of patients who have discontinued XYWAV or XYREM after receiving at least one shipment of XYWAV or XYREM. Include demographics of discontinued patients and reasons for discontinuation.
 - iv. Number and percentage of patients who transitioned from XYREM to XYWAV
 - v. Number and percentage of patients who transitioned from XYWAV to XYREM.
 - b. Healthcare Providers:
 - i. Number and percentage of newly certified healthcare providers stratified by professional designation (i.e. MD, DO, PA, NP), medical specialty, and geographic region (defined by US Census)

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- ii. Number and percentage of active certified healthcare providers (healthcare providers who have written at least one prescription for XYWAV or XYREM during the reporting period) stratified by professional designation (i.e. MD, DO, PA, NP), medical specialty, and geographic region (defined by US Census)
 - iii. Number of patients by current enrolled prescriber.
 - c. Certified Pharmacy
 - i. If the Certified Pharmacy was decertified during the reporting period and reasons for decertification.
 2. Utilization Data (per reporting period and cumulatively)
 - a. Number and percentage of XYREM prescriptions (new and refills) dispensed
 - b. Number and percentage of XYWAV prescriptions (new and refills) dispensed
 - c. Number and percentage of XYREM bottles and shipments sent
 - d. Number and percentage of XYWAV bottles and shipments sent.
 3. REMS Program Operation and Performance Data (per reporting period and cumulatively)
 - a. REMS Program Central Database Report
 - i. Number and percentage of contacts by stakeholder type (e.g. patients, healthcare providers, pharmacy, other)
 - ii. Summary of reasons for contacts (e.g., enrollment questions) by reporter (authorized representative, patient, healthcare provider, other)
 - iii. Call center report with number of calls received and a summary of reasons for calls by stakeholder type
 - iv. Summary of frequently asked questions by stakeholder type and topic
 - v. Summary of any REMS-related problems identified and a description of any corrective actions taken
 - vi. If the summary reason for the calls indicates a complaint, provide details on the nature of the complaint(s) and whether they indicate potential REMS burden or patient access issues
 - vii. Summary of program or system problems and a description of any corrective actions taken.
 4. REMS Program Compliance (per reporting period and cumulatively)
 - a. Audits: Summary of audit activities including but not limited to:
 - i. A copy of the audit plan for each audited stakeholder.
 - ii. The number of audits expected, and the number of audits performed
 - iii. The number and type of deficiencies noted

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- iv. For those with deficiencies noted, report the status of corrective and preventative action (CAPA) proposed to address the deficiencies. The status to include completion status.
 - v. For any that did not complete the CAPA within the timeframe specified in the audit plan, describe actions taken
 - vi. Provide details on deviations for the CAPA proposed, including timelines, and mitigating steps to address the deviations
 - vii. Confirm documentation of completion of training for relevant staff
 - viii. Review of accumulative findings to identify any trends of potential repeat issues, and steps to be taken to address these findingsA summary report of the processes and procedures that are implemented to be in compliance with the REMS requirements.
- b. A summary report of noncompliance, associated corrective and preventive actions (CAPA) plans, and the status of CAPA plans including but not limited to:
- i. A copy of the Noncompliance Plan which addresses the criteria for noncompliance for each stakeholder, actions taken to address noncompliance for each event, and under what circumstances a stakeholder would be suspended or de-certified from the REMS
 - ii. The number of instances of noncompliance accompanied by a description of each instance and the reason for the occurrence (if provided). For each instance of noncompliance, report the following information:
 - 1) The unique ID(s) of the stakeholder(s) associated with the noncompliance event or deviation to enable tracking over time
 - 2) The source of the noncompliance data
 - 3) The results of root cause analysis
 - 4) What action(s) were taken in response.
- c. Healthcare Providers
- i. Number and percentage of certified prescribers who were disenrolled during the reporting period and reasons for disenrollment. Include if any prescribers were re-certified.
 - ii. Number of disenrolled prescribers who were associated with a XYWAV and XYREM prescription and number of disenrolled prescribers associated with a XYWAV and XYREM shipment

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- iii. Number and percentage of XYWAV prescriptions filled from a prescriber who was not enrolled.
- iv. Number and percentage of XYREM prescriptions filled from a prescriber who was not enrolled.
- d. Certified Pharmacy
 - i. Number and percentage of XYWAV prescriptions dispensed for more than a 30 days' supply (first fill) or more than a 90 days' supply (refills) and reasons
 - ii. Number and percentage of XYREM prescriptions dispensed for more than a 30 days' supply (first fill) or more than a 90 days' supply (refills) and reasons
 - iii. Number and percentage of XYWAV shipments lost in delivery (and unrecovered) with number of DEA 106 Forms and Risk Management Reports (RMRs) completed
 - iv. Number and percentage of XYREM shipments lost in delivery (and unrecovered) with number of DEA 106 Forms and Risk Management Reports (RMRs) completed
 - v. Number and percentage of initial XYWAV shipments sent to patients without completion of the XYWAV and XYREM REMS Patient Counseling Checklist.
 - vi. Number and percentage of initial XYREM shipments sent to patients without completion of the XYWAV and XYREM REMS Patient Counseling Checklist.
- e. Patients
 - i. Number and percentage of patients who were disenrolled from the program and reasons for disenrollment
 - ii. Number and percentage of patients associated with more than one prescriber during their therapy
 - iii. Number and percentage of patients prescribed a daily dose of XYWAV of >9 g
 - iv. Number and percentage of patients prescribed a daily dose of XYREM of >9 g
 - v. Number and percentage of patients with overlapping prescriptions (more than one active prescription shipped)
 - vi. Number and percentage of patients with concurrent XYWAV and XYREM prescriptions
 - vii. Number of duplicate patients detected by the Certified Pharmacy

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- viii. Number and percentage of duplicate patients who were shipped XYWAV or XYREM under more than one name or identifier
- ix. Number and percentage of patients who were shipped XYWAV or XYREM after being disenrolled
- x. Number and percentage of patients who requested an early refill of XYWAV and reason for the request
 - 1) Number and percentage of requests approved
 - 2) Number and percentage of requests denied by the prescriber
 - 3) Number and percentage of requests denied by the Certified Pharmacy
 - 4) Number and percentage of patients with multiple requests for early refills.
- xi. Number and percentage of patients who requested an early refill of XYREM and reason for request
 - 1) Number and percentage of requests approved
 - 2) Number and percentage of requests denied by the prescriber
 - 3) Number and percentage of requests denied by the Certified Pharmacy
 - 4) Number and percentage of patients with multiple requests for early refills.

Safe Use Behaviors

- 5. Pharmacy Notifications (per reporting period and cumulatively, for both XYWAV and XYREM)
 - a. A summary of the notifications by pharmacies to prescribers for both XYWAV and XYREM. For each of the following situations, include the number and percentage of notifications, number of unique patients, the outcome of the pharmacy notification (e.g. counseled patient, discussed with prescriber and prescriber's designee) and outcome of XYWAV and XYREM prescription disposition (e.g. prescriber approved shipment, prescriber requested shipment hold, prescriber denied shipment, pharmacy approved shipment):
 - i. Use with sedative-hypnotics indicated for sleep (e.g., eszopiclone, zaleplon, zolpidem, temazepam, suvorexant, quazepam, estazolam, flurazepam, triazolam, tasimelteon, ramelteon). Indicate specific actions taken by the prescriber and the prescriber rationale for continuing treatment in response to the notification including the following:
 - Treatment with XYWAV /XYREM will discontinue
 - Sedative hypnotic will be discontinued

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- Dosage of sedative hypnotic has been/will be reduced
 - Information unavailable
 - No action (continue sedative hypnotic with XYWAV or XYREM)
 - Prescriber's rationale for continued use of sedative hypnotic with XYWAV or XYREM
 - o Sedative hypnotic will not be taken at the same time as XYWAV /XYREM
 - o Sedative hypnotic will be taken at the same time as XYWAV /XYREM
 - o Sedative hypnotic will be taken as a sleep aid
 - o Sedative hypnotic will be taken for different indication per medical need
 - o XYWAV /XYREM dose regimen changed
 - o No rationale provided
- ii. Benzodiazepines (e.g., diazepam, alprazolam or any not listed in metric 5.a.i.). Indicate specific actions taken by the prescriber and the prescriber rationale for continuing treatment in response to the notification including the following:
- Treatment with XYWAV /XYREM will discontinue
 - Benzodiazepine will be discontinued
 - Dosage of benzodiazepine has been/will be reduced
 - Information unavailable
 - No action (continue benzodiazepine with XYWAV or XYREM)
 - Prescriber's rationale for continued use of benzodiazepine with XYWAV or XYREM
 - o Benzodiazepine will not be taken at the same time as XYWAV /XYREM
 - o Benzodiazepine will be taken at the same time as XYWAV /XYREM
 - o Benzodiazepine will be taken as a sleep aid
 - o Benzodiazepine will be taken for different indication per medical need
 - o XYWAV /XYREM dose regimen changed
 - o No rationale provided

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- iii. Use with other concomitant CNS-depressant medications (sedating antidepressants or antipsychotics, sedating anti-epileptics, sedating antihistamines, general anesthetics, muscle relaxants, opioid analgesics, or illicit CNS depressants)
 - iv. Patient report of alcohol use
 - v. Patient report of diagnosis of sleep apnea
 - vi. Patient report of diagnosis of asthma, COPD, or other conditions affecting breathing
 - vii. Suspected abuse, misuse, or diversion
 - viii. Alerts regarding potential abuse, misuse, or diversion on the patient profiles
 - ix. Prescription error
 - x. Early refill requests
6. Risk Management Reports (RMRs) (per reporting period and cumulatively, for both XYWAV and XYREM)
- a. Number and percentage of RMRs submitted
 - b. Number and percentage of unique patients with a RMR
 - c. Number and percentage of unique patients with multiple RMRs
 - d. Number and percentage of alerts generated from RMRs
 - e. Number and percentage of RMRs generated from early refill requests
 - f. Number and percentage of RMRs generated for other reasons (list reasons)
 - g. Number and percentage of prescriber-related RMRs
 - h. Number and percentage of RMRs that included an adverse event.
7. REMS Program Patient Counseling Checklist (per reporting period and cumulatively, for both XYWAV and XYREM)
- a. Summary table for both XYWAV and XYREM from REMS Program Patient Counseling Checklists of the number and percentage of patients taking the following concomitant medications and who subsequently received at least one shipment of drug:
 - i. Sedative hypnotics indicated for sleep (e.g., eszopiclone, zaleplon, zolpidem, temazepam, suvorexant, quazepam, estazolam, flurazepam, triazolam, tasimelteon, ramelteon)
 - ii. Alcohol
 - iii. Other potentially interacting agents:
 - Benzodiazepines (e.g., diazepam, alprazolam or any not listed in metric 7.a.i.)
 - Sedating antidepressants or antipsychotics, sedating anti epileptics, and sedating antihistamines
 - General anesthetics
 - Muscle relaxants

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- Opioid analgesics
 - Divalproex sodium or other valproate drug (e.g., valproic acid)
 - Illicit CNS depressants (e.g., heroin or gamma-hydroxybutyrate [GHB]).
- b. Summary tables for both XYWAV and XYREM from REMS Program Patient Counseling Checklists of the number and percentage of patients who have been diagnosed with the following conditions and who subsequently received at least one shipment of drug:
- c. Sleep apnea
- d. Asthma, COPD, or other conditions affecting the respiratory system.

Health Outcomes and/or Surrogates of Health Outcomes

8. Pharmacovigilance/surveillance (per reporting period)
- a. Separate summary tables for XYWAV and XYREM of the number of reports of serious adverse events. The summary tables will include the following data fields (CIOMS II line listings): date, report ID, report type, notifier, age, gender, indication, start and stop date, dose, frequency, onset date, system organ class, outcome, and causality. All tables should include an overall narrative summary of the adverse events and data fields reported.
- i. All cases of death
 - 1) Number, percentage, and type of RMRs, notifications, and alerts associated with any reported deaths.
 - ii. All outcomes of death, emergency department visits (when admitted to hospital), or hospitalizations resulting from or associated with the following:
 - 1) Use with concurrent sedative hypnotics and alcohol. Provide a breakdown of concomitant sedative hypnotics usage (ex. zolpidem=6%, eszopiclone=3%)
 - 2) Intentional misuse
 - 3) Abuse
 - 4) Overdose
 - 5) Medication error
 - iii. Cases of sexual abuse
 - iv. Proportion of discontinued patients who were associated with a report of a serious adverse event, including death.

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Knowledge

9. Knowledge, Attitude, and Behavior (KAB) Surveys of Patients, Caregivers, and Healthcare Providers (to be submitted every other year beginning with the April 2023 assessment)
 - a. Assessment of patients'/caregivers' and healthcare providers' understanding of the following:
 - i. The risk of significant CNS and respiratory depression associated with XYWAV and XYREM even at recommended doses
 - ii. The contraindicated uses of XYWAV and XYREM
 - iii. The potential for abuse, misuse, and overdose associated with XYWAV and XYREM
 - iv. The safe use, handling, and storage of XYWAV and XYREM
 - v. The XYWAV and XYREM REMS Program requirements.
10. Knowledge, Attitude, and Behavior (KAB) Surveys of Pharmacists (to be submitted every other year beginning with the April 2023 assessment)
 - a. Assessment of pharmacists' understanding of the following:
 - i. The risk of significant CNS and respiratory depression associated with XYWAV and XYREM even at recommended doses
 - ii. The contraindicated uses of XYWAV and XYREM
 - iii. The potential for abuse, misuse, and overdose associated with XYWAV and XYREM
 - iv. The safe use, handling, and storage of XYWAV and XYREM
 - v. The XYWAV and XYREM REMS Program requirements.
11. Certified Pharmacy knowledge assessments (per reporting period and cumulatively)
 - a. Number of pharmacy staff who completed post-training knowledge assessments including method of completion and the number of attempts needed to complete.
 - i. Provide a breakdown of scores within Module A and B
 - b. Summary of the most frequently missed post-training knowledge assessment questions
 - c. Summary of potential comprehension or perception issues identified with the post-training knowledge assessment by module
 - d. Number of pharmacy staff who did not pass the knowledge assessments.
12. The requirements for assessments of an approved REMS under section 505-1 (g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each

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element of the strategy, is meeting the goal or whether one or more such goals or such elements should be modified.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.
- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications,* provide a rationale for why the REMS does not need to be modified.

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If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA ##### REMS ASSESSMENT METHODOLOGY
(insert concise description of content in bold capital letters, e.g.,
ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES,
AUDIT PLAN, DRUG USE STUDY)**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA ##### REMS ASSESSMENT

or

**NEW SUPPLEMENT FOR NDA #####/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR NDA #####/S-000
PRIOR APPROVAL SUPPLEMENT**

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PROPOSED MAJOR REMS MODIFICATION

or

**NEW SUPPLEMENT FOR NDA #####/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING
CHANGES SUBMITTED IN SUPPLEMENT XXX**

or

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA #####/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA #####

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, or website screenshots are only in PDF format, they may be submitted as such, but Word format is preferred.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-*

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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*Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*³

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact Teresa Wheelous, Regulatory Project Manager, at teresa.wheelous@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Acting Director
Division of Neurology 1
Office of Neuroscience
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - o Prescribing Information
 - o Medication Guide
 - o Instructions for Use
- REMS

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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EXHIBIT 16

Q3 2024 Earnings Call *(Raw version)*

✓ **Event Details**

Date: 2024-11-12
Company: Avadel Pharmaceuticals Plc
Ticker: AVDL-US

✓ **Company Participants**

Unverified Participant
Gregory J. Divis - Avadel Pharmaceuticals Plc, Chief Executive Officer & Director
Thomas S. McHugh - Avadel Pharmaceuticals Plc, Chief Financial Officer

✓ **Other Participants**

David Amsellem - Analyst

MANAGEMENT DISCUSSION SECTION

Operator

Good day, everyone, and welcome to today's Avadel Pharmaceuticals 3Q 2024 Earnings Call. At this time, all participants are in a listen-only mode. Later, you will have the opportunity to ask questions during the question-and-answer session. Please note this call is being recorded and I will be standing by if you should need any assistance.

It is now my pleasure to turn the conference over to Austin Murtagh with Precision AQ.

Unverified Participant

Good morning, and thank you for joining us on our conference call to discuss Avadel Pharmaceuticals Third Quarter 2024 results.

As a reminder, before we begin, the following presentation includes several, several matters that constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those contemplated in such forward-looking statements. These risks and uncertainties are described in Avadel's public filings under the Exchange Act included in the Form 10-K for the year ended December 31, 2023, which was filed on February 29, 2024, and subsequent SEC filings. Except as required by law, Avadel undertakes no obligation to update or revise any forward-looking statements contained in this presentation to reflect new information, future events or otherwise.

On the call today are Greg Divis, Chief Executive Officer; Richard Kim, Chief Commercial Officer; and Tom McHugh, Chief Financial Officer. Dr. Jennifer Gudeman, Senior Vice President of Medical and Clinical Affairs, will additionally join us for the Q&A portion of the call.

At this time, I'll turn the call over to Greg.

Gregory J. Divis

Thank you, Austin. Good morning, everyone, and thank you for joining us. Following my opening remarks, Richard will provide an update on our commercial progress, and Tom will then review our third quarter financial results. We will then conclude with a question-and-answer session. As we begin today's call, let me start by summarizing our Q3 results, another quarter where once again we delivered consistent patient growth and a LUMRYZ launch while making progress across a number of additional important fronts.

As we detail our launch results today, including our key metrics and how our source of new LUMRYZ patients continue to advance, it is clear that we have begun to make a real impact on the patients we are serving with the full recognition that we are moving to the next phase of our launch. And as such, there remains much work to be executed to deliver on the full promise and potential of LUMRYZ for all stakeholders.

Turning to the launch metrics that Richard will cover in more detail shortly. We reported there were 2,300 active patients on therapy as of September 30, and 700 patients who initiated LUMRYZ therapy in Q3, resulting in \$50 million in net revenue during the third quarter. More specifically, during Q3, we saw the following trends. First, we see continued strong representation from all three patients segments, switch, new to oxybate and previously treated and discontinued patients. Switch patients continue to make up the largest portion of new patients status in Q3, with most switches coming from the mix of oxybate product, a trend that has continued since the beginning of launch.

Second, patients who are new to oxybate represent the fastest growing segment of LUMRYZ patient starts. Which is coming from both existing oxybate prescribers as well as prescribers who have never written an oxybate prior to LUMRYZ availability. And lastly, we believe these data points are important leading indicators of the potential emerging signs of expansion in the overall market which despite not being a core focus of our initial launch, is happening even earlier than we had previously anticipated. With this emerging expansion of new to oxybate patient demand, it's important to note that based on historical twice-nightly oxybate trends and our early LUMRYZ launch data, we can expect to see lower persistency rates in this new to oxybate patient population.

Richard will provide more detail on this and the actions we are taking in this regard as we are making additional investments to support all patients transitioning onto LUMRYZ. Furthermore, in October, we were pleased to announce receipt of FDA approval and orphan drug exclusivity for Lumryz in treating cataplexy or excessive daytime sleepiness in pediatric patients seven years and older with narcolepsy. As with adult patients, LUMRYZ is determined to be clinically superior to the twice-nightly products in the pediatric patient population based on its major contribution to patient care.

Specifically FDA stated Lumryz's dosing provides an opportunity to minimize sleep fragmentation and disruption of sleep architecture in a way that is not possible for a patient on a twice-nightly dosing regimen of oxybate. FDA went on to say this is medically relevant because the goal for treating patients with sleep disorders is to restore normalcy pattern and a healthier sleep physiology. We've always recognized, based on direct feedback from providers, patients and their families, the burdens and limitations that first generation oxybate have on children with narcolepsy and their caregivers. We're proud to be able to offer Lumryz to all eligible people with narcolepsy, and in this regard, Lumryz is commercially available and is currently being prescribed to and used. Lastly, turning into our indication and portfolio expansion efforts, enrollment is ongoing in our Phase 3 REVITALYZ study, which we are evaluating, LUMRYZ's potential clinical benefit in adults with idiopathic hypersomnia or IH. We asked significant clinicians that IH patients have difficulty physically waking up to their second dose given the deep sleep inertia associated with our IH. So potentially having new lines available for IH patients is not only important but also very much needed. In addition to our IH phase 3 study, we continue the preclinical development of our low sodium once-at-bedtime oxybate formulations seeking a target product profile that is bioequivalent to LUMRYZ and meets all FDA required standards. As this program remains in early preclinical formulation development stages, we will plan to provide future updates as and when these programs advance.

Beyond our commercial and clinical progress we recently announced the District of Columbia Court's favorable ruling affirming the FDA's approval and clinical superiority decision for LUMRYZ based on its unique once nightly dosing profile. We are pleased that this ruling for a number of reasons as we continue executing our launch while mitigating an important legal and business risk for the company. In summary, the third quarter represented another consistent quarter of LUMRYZ execution, bolstered by additional key developments. The pediatric approval, along with the Second Orphan Drug Exclusivity Award granted by FDA for LUMRYZ. The initiation of our IH phase 3 trial and the affirmative court decision in the District of Columbia ATA litigation. As we look toward 2025 with a clear vision for growth, we remain focused on executing the near-term value drivers, including the continued launch of LUMRYZ and our lifecycle management efforts, all in our pursuit of realizing the full potential of LUMRYZ for all stakeholders. I'll now turn the call over to Richard for details on our launched products. Richard?

Unverified Participant

Thank you and good morning, everyone. Echoing Greg's earlier sentiments it continues to amaze is how much of an impact the embrace has made across the narcolepsy community. And I'm excited to be here this morning to discuss our commercial launch in more detail. At the end of the third quarter, we had 2,300 patients on therapy. We also saw a solid pace of new patient starts with 700 patients with initiate therapy in third quarter showing that demand has been consistent.

Turning to the patient segments, we have always believed that growth for Oxybate in narcolepsy will be driven by growing in you two oxybate patients. And now we are seeing the new to Oxybate segment emerge at the fastest growing segment per patient initiations. Per patient switching from first generation oxybate to LUMRYZ launched today. There are largest group of initiations and patients on therapy. They will continue to be a key patient segment as the comparative value proposition for once at that time dosing is extremely compelling for these patients. We have also seen a consistent transporter reporter with patients who have tried and previously discontinued oxybates. With the growth in the new to oxybates segment, this does have an impact in terms of the overall persistency for patients on LUMRYZ.

First. And importantly, based on the data we have, we see that LUMRYZ has overall improved persistency compared to 2018 oxybate. This is for both the switch and the new out of oxybate patients. However, not surprisingly, we are seeing lower persistency rates in new to oxybate patients versus switch patients. When patients do not have prior experience with oxybate and are not clear that it can take some time to find their optimal dose while balancing tolerability, this can lead to earlier and higher rates of discontinuation. These patients need more frequent engagement, especially during the first several weeks of This can lead to earlier and higher rates of discontinuation. These patients needed more frequent engagement, especially during the first several weeks of therapy. We started to make key investments to address persistency. These efforts include doubling the number of Nurse Care Navigators that rise up and increasing their overall education efforts regarding tolerability and efficacy. In addition, we've increased the cadence for patient engagement not only from rise up but also from the specialty pharmacies. We are also doubling our field team that supports both officers and patients in initiating and refilling the rise.

From an ACP perspective, we continue to LUMRYZ writers in the highest volume oxybate prescribers. There are about 500 ACPs that make up 50% of the market volume, and we are pleased that at September 30th that 90% graded for LUMRYZ. We also continue to see more lower volume oxybate prescribers begin to write for LUMRYZ and treat more eligible patients, and part of the LUMRYZ availability. Additionally, we have seen a continued expansion of health care practitioners who had never written for an oxybate fire not right for LUMRYZ. This group now represents about 150 providers, which is up from more than over 100 last quarter. For these reasons, we have made the decision to expand our sales team, to increase our coverage and frequency with moderate and lower volume oxybate prescribers, as well as targeted prescribers who have previously not used oxybate. While at the same time maintaining our continued focus on the high volume prescribers.

We believe these moderate, low and new prescriber groups represent an initial wave of growth and opportunity for continued market expansion. Based on what we have seen thus far in the launch. Further, we are also excited for and have already been executing against the recent approval from LUMRYZ and pediatric narcolepsy patients seven years of age and older. To close, we had another consistent quarter of increases in patient starts and we have built a solid foundation for our launch going forward.

Now successful launches are all about listening, learning and adapting. And we are now in a new phase of the launch that comes with new challenges and new opportunities. There are dynamics in the launch with the source of patient initiations being driven more by new to oxybate patients. And what comes with these patients is lower persistency rates, which can potentially impact the rate of quarter-over-quarter growth in net patient ads. We are making additional investments that we believe will drive demand, product fulfillment and improve persistence rate over the long run. The additional investments are with a clear goal to maximize the amazing opportunity we have from LUMRYZ to become the preferred oxybate among people with narcolepsy and providers.

Now I will turn the call over to Tom for an update on our financial results. Tom?

Thomas S. McHugh

Thank you, Richard. Before I begin, please note that full financial results are available on the press release issued this morning in the 10-Q. I will also be reviewing non-GAAP financial results, which can be found on our Investor Relations website at investors.avadel.com.

I'll start with our top line results. In the quarter ended September 30, we reported net revenue of \$50 million and gross profit of \$43.9 million and we estimate the number of weeks of inventory in the channel at September 30 was approximately the same as June 30. With respect to gross profit, I'll further note that cost of goods sold includes a onetime adjustment for an estimated potential royalty on sales of LUMRYZ for the period February 2024 through June 2024 related to the ongoing litigation with jazz, which impacted gross margin by approximately 3.5%. Adjustment was reported as a non-cash true-up in the quarter ended September 30. While we await a final disposition of that matter, and any related appeals, this potential royalty has no near-term impact on cash, and we expect that gross margin going forward will be greater than 90%, including an estimate of a potential ongoing royalty.

Turning to operating expenses, we reported \$44.2 million of GAAP operating expenses for the third quarter, which includes \$6.4 million of non-cash charges comprised of stock-based compensation of \$5.4 million and depreciation and amortization of \$1 million. After adjusting for these items, cash operating expenses were \$37.8 million. And we expect that recurring quarterly cash operating expenses for the fourth quarter will be in the range of \$40 million to \$45 million, which includes the additional patient and provider support investments, Richard noted earlier. And non-cash operating expenses will be in the range of \$6 million to \$7 million.

With respect to the balance sheet, we had approximately \$66 million of cash, cash equivalents and marketable securities as of September 30 compared to \$71 million as of June 30. The net use of cash during the quarter included \$2 million, the payment of a commitment fee due to not exercising the option to draw the second royalty tranche, one of the royalty pricing agreement we entered into at the beginning of 2023.

With respect to achieving operating breakeven, we were just shy on a gap basis with an operating loss of \$327,000. After adjusting for non-cash operating expenses, adjusted EBITDA calculated its gross profit of \$43.9 million minus cash operating expenses of \$37.8 million was a positive \$6.1 million.

And as we look ahead to Q4, in entering the holiday season we expect potential seasonal impacts, which include that patients may not visit their provider during the typical cadence and fewer shipping days.

Furthermore, we expect higher gross to net deductions, which will primarily impact inventory in the channel at December 31 given the insurance plans, reset deductibles and increase co-locate assistance in the New Year. Finally, based on our current plans and assumptions, we expect that cash flow will be positive during the fourth quarter. Our expectations regarding financial results in the fourth quarter are based on a number of factors, including the number of reimbursed patients on LUMRYZ, net pricing on LUMRYZ, cash operating expenses and the seasonality factors I mentioned a few moments ago. And with that, I'll turn the call back to Greg for closing remarks.

Unverified Participant

Thank you, Tom. Q3 of third quarter marked by a number of achievements and consistent progress across a number of key areas. As we continue to execute on our launch and build our patient base, expanded the eligible target treatment population to LUMRYZ pediatric approval, we've initiated our Phase 3 IH trial and we secured a favorable and strategically important court decision from the DC court. With this substantial progress behind us and our transition into the next phase of the LUMRYZ launch, we believe we have built the foundation required to be on our way to transforming patient care for narcolepsy patients and fulfilling the promise of LUMRYZ for all stakeholders. As always, we thank you for your support and we look forward to providing future updates on our progress. With that, we will open the call for questions. And I'll turn it back to the operator.

QUESTION AND ANSWER SECTION

Operator

We will pause for a moment to allow questions to queue. And we'll take our first question Andrew Tsai with Jefferies. Your line is open.

Unidentified speaker

Question – Unidentified speaker: Hey, good morning. Thanks for taking my questions. I appreciate the update. Can you talk about the patient trends you're seeing so far, including the month of October and the parts of November? And your confidence around a strong Q4 growth trajectory, despite, I think in your prepared remarks, some potential seasonality and higher gross to net deductions? And are you still confident you will continue gaining share from former OXYBATE users as well as existing switches, not just the naïve Oxybate group? Thanks.

Answer – Unidentified speaker: Thanks Andrew. Richard.

Answer – Unidentified speaker: Yeah. Hey, good morning Andrew. Thanks for the question. Yeah, thus far, I mean, we continue to see strong demand for LUMRYZ in this quarter as well. I think what Thomas commented on is just it's a shorter quarter as far as selling days and office visits and things like that. But interest in demand for LUMRYZ remains very strong still. And as far as sourcing business from switch patients, absolutely we continue to see that as a core part of the business going forward. We have just seen some of a new dynamic with the trends for where we are right now in the launch. But the switch patients from the twice-nightly oxybate will continue to remain a very important part of our business going forward because the value proposition there is very compelling.

Unidentified speaker

Question – Unidentified speaker: Great. Thanks.

Operator

Thank you. We'll take our next question from Francois Brisebois with Oppenheimer. Your line is open.

Unidentified speaker

Question – Unidentified speaker: Hey, thanks for the question. Just the first one in terms of the new to oxybate, can you just help us understand with the 00:19:35 and going forward how that works in terms of insurance? Is there a step through to kind of deal with this in this new stage of the launch. Can you just help us understand how much you're going to grow the sales force or just maybe a hierarchy of what's the most important thing to work on here to adapt to this new reality?

Answer – Unidentified speaker: Yeah, thanks, Frank. I think your first question centered around the role of AGs relative to New-to-Oxybate. And then how are we going to expand and continue to invest in our launch as it continues to progress. So, Richard?

Answer – Unidentified speaker: Yeah, as far as the New-to-Oxybate and any AG is Frank, our plan right from the beginning as far as the peers were concerned was to get ready access with the best of the oxybate. We have – the team has done a really excellent job with that with 85% commercial coverage. So it's very rare that an AG is a step for LUMRYZ for hypersomnia. So we see that care pathway to new-to-oxybate patients is very robust for us. And as far as the salesforce is concerned, maybe I'll step back and sort of say, when we first launched, our goal was clearly to get uptake with the highest volume oxybate prescribers and with 90% who have written through the third quarter, we feel like we've done a really good job with that.

It's really that time now to continue to add to grow more it was moderate and low oxybate users. So we're adding a little over 10% of our field force into the mix right now to increase our reach and frequency to those providers. And also, as we stated in our prepared remarks, we're getting people who had never returned Oxybate before who for REVITALYZ and LUMRYZ, about 150 of those now launched to date. So we also would be targeting a select group of those to increase our mix of new REVITALYZ and LUMRYZ as well.

Answer – Unidentified speaker: Yeah. And I think the only comment I would add is that across these moderate to low prescribers, without compromising our focus and efforts on the highest value targets, there are also switch patients that exist in those practices as well. So I think the source of patient is – doesn't change for us in terms of new-to-oxybate previously treated and discontinued or switch patient in particular in current oxybate prescribers right. I think where we're adding some people to provide some additional coverage is in those physicians and physicians that look a lot like those physicians who have made the decision to write and treat with LUMRYZ who have never before used an oxybate predominantly based upon the dosing issues that they didn't want to have to deal for their patients.

Unidentified speaker

Question – Unidentified speaker: Okay, great. And then maybe for Tom, you know, you would talk about how you're tracking the sell-side. And I think on the last call, I think for the year, it looked like \$168 million was the sell-side consensus on the revenues. I know you're not giving guidance, but any comment in terms of revenues and the sell-side? And then I guess maybe lastly, you know, there's been a lot of developments on the litigation front. I think maybe just an update on what's next what is still up there in terms of litigation would be helpful. Thank you.

Answer – Unidentified speaker: Thanks, Frank. I'm happy to handle the legal time if you want to start but...

Answer – Unidentified speaker: Yeah. Sure, no, thanks for the question, Frank. Appreciate it. You know, I think with respect to expectations in Q4, we're really pleased with the progress to-date through the first five full quarters of launch. And we do expect to see continued and consistent patient demand for LUMRYZ across all patient segments. And with that said, we have seen an increase in the new to Oxybate patient segment, which which has impacted persistency that we're in the process of assessing. So as we're looking into Q4 and our expectations for Q4, we're evaluating, you know, the growth in new to Oxybate segment. It's looking quite effective as well as seasonality factors I mentioned during the call.

Answer – Unidentified speaker: And Frank as it relates to legal, maybe I'll just kind of tick through kind of where things are from a legal perspective. First, obviously, as we noted, we're pleased with the DC court's decision, which aligns with what we have stated all along from that perspective. On the other legal matters, which are really Delaware related. Really there's three. The first one is the ongoing patent trial, for which the next steps in that case are anticipated to include, you know post-trial motions that whole process, as well as a briefing and a hearing regarding the future ongoing royalty rate. Neither of those have been scheduled yet. So that is pending, right. There's the IH injunction, which is under appeal at the federal circuit. And briefing, for that matter, is scheduled to be complete next week, with oral arguments currently scheduled for the February 2025 docket, but a date not yet set.

And then lastly and equally as important is our antitrust action against Jazz that's progressing and across, you know in accordance to what needs to occur during this period of time. And I'll just remind everybody that, you know, that is really about what we believe to be wrongfully delayed during the NDA review process based upon the wrongfully listed REMS patents and the impact that has had and that is currently scheduled with a jury trial beginning November 3 of next year. So that's where we sit on the legal matters.

Unidentified speaker

Question – Unidentified speaker: Thank you. Sorry if I can just jump in here, your recent win with the District Court of Columbia in terms of clinical superiority, can that read through to the appeal that you guys have with IH or are we just is it are we not discussing that?

Answer – Unidentified speaker: Yeah. I don't think it's appropriate to comment on the specifics of that other than that, you know we're pleased that the FDA has now granted us an orphan exclusivity twice. And the court the DC court has affirmed that decision. And what the FDA came to that decision.

Unidentified speaker

Question – Unidentified speaker: All right. Thank you. And congrats on the quarter.

Operator

Thank you. We'll take our next question from Oren Livnat of H.C. Wainwright. Your line is open.

Unidentified speaker

Question – Unidentified speaker: Thanks for taking the questions. So since your new patients starts are actually running ahead of our expectations, but obviously the discontinuations is something we're digging into more. So just can you talk about why new patients are discontinuing more, I mean, you talked about

education, about tolerability and dose titration. Is there actually any difference, do you believe, in the tolerability for these patients and versus long time users of twice-nightly? Or is it really just that every new patient is always more challenging? And I guess is the support services that you offer from, rise up are more important on an ongoing basis sort of long term to hold their hand? Or is it really just about expectation setting upfront and doing a better job there? And I think someone asked about reimbursement for new patients. Do you see any issues with reauthorizations being needed early on? And that is a source of new patient discontinuations as well. And I have a follow up. Thanks.

Answer – Unidentified speaker: Yeah. Yeah, Thanks Oren a lot there, so maybe Richard you can start.

Answer – Unidentified speaker: Yeah. Sorry. Yeah. No. I'm really sorry. So, yeah, No, as far as the higher discontinuation rates, I think the biggest way we would really sort of frame this is a lot of patients who are never been oxybate, they just don't know what to expect. Right. Consider they come from 00:27:19 who wait for money agents that can work very quickly and new to oxybate patients they need to find their optimal dose overall. A lot of physicians actually do set expectations, but we also found find market research many do not. And also there's a lot of information generally to start with patients. So the nurse care navigators is the right player – in it's essential role in really helping support patients, really in managing expectations and helping them know what to expect, knowing that it may take several weeks for your efficacy to really kick in and knowing that as you need – changed your dose you may experience some more tolerability issues. So we see the nurse care navigators as not only critical at the beginning, but really in building those relationships with patients longer term as well. That's really why we've made the investments politically across the board there and also when it comes to reimbursement for the patients, it's maybe not so much the reauthorizations for some of these patients. They do come to the mix from time to time. But clearly for these patients and others, there are patients who may change their insurance from time to time that can have an impact. So overall, the reimbursement and payer mix can have an impact. But I think for the new to Oxybate patients, it's really about establishing expectations, providing much more frequent support for them and being there not only at the beginning but through their whole journey of treatment as well.

Answer – Unidentified speaker: Yeah, I think the only thing I would add Oren to Richard's comment is that, you know, as we've gone through the launch and we and our source of business has changed, we've had to get, you know, and we've gotten smarter. We've got much more kind of precise or surgical in how we engage different patient types, right? Because what happens with a switch patient and how you're helping them manage persistency is different early on in their experience that we're managing it is with a new to oxybate patient. So kind of a one size fits all doesn't really work in totality. So we've gotten much more sophisticated in that regard. And as a result of that, we've expanded our nurses that allows them to reduce their caseload and spend more time with patients as required to help them navigate through these periods of time. So again, we have, you know, we think the right insights, taking the right actions and have the ability to impact it.

And, you know, I think all of our data to date has demonstrated that although we have better discontinuation rates relative to the historical trade navy trends. It's just, you know, it's not -- it's not the right standard. We wanted to do better than that. Because we work really hard to get a patient on therapy and we want to help them stay in.

Unidentified speaker

Question – Unidentified speaker: Yes. And regarding reimbursement in general, have there been any material changes going or are there any material changes going into 2025, both in terms of standalone coverage and maybe relative formulary positioning versus competition? And how much of a tailwind should Medicare coverage be in 2025 and beyond? And just overall, can you remind us where you stand on, I guess, an annualized net value for patients now and going forward. And does that already sort of bacon bridging or free drug supply or is that just a separate line item? Thanks.

Answer – Unidentified speaker: Right. You want to. Richard, take the first part.

Answer – Unidentified speaker: Sure. Yeah. We're super pleased with the coverage that we have with the . We don't want to tip our hand totally, but we expect that to have very strong coverage as we go into 2025 across the board. And in 2025, we should pick up some more Medicare lives overall. And so we believe ending 2024 and 2025, we will be in a very strong position as far as our overall coverage is concerned.

Answer – Unidentified speaker: Yeah. In terms of net value for patient, do you think you can calculate off the numbers from the report and which -- which patient numbers were reporting such patients on free drugs? But with that said, or in the -- the average net revenue per patient is right around \$100,000 on an annualized basis. The complexity a little bit, you know, quarter to quarter, but generally speaking, about \$100,000 per year per patient, including patients on treatment.

Unidentified speaker

Question – Unidentified speaker: Perfect. Thanks so much. I don't want to be greedy. I'll hop back in a queue.

Operator

Thank you. We'll take our next question from Ami Fadia with Needham. your line is open.

Unidentified speaker

Question – Unidentified speaker: Hi. Good morning. Thanks for taking my question. Can you talk about what percent of new patient starts currently you're seeing that are coming from completely new patients versus switch patients? And in terms of switch patients, can you give us some color around the dynamics in terms of whether they're coming from the high sodium Xyrem or their 00:32:04 or the low sodium oxybate? And as you think about investing behind more detailing efforts here, can you just talk about how the growth rate of the overall oxybate market has evolved since the launch of Lumryz? Thank you.

Answer – Unidentified speaker: Okay. I'll say something. Maybe I'll make some comments and turn over Richard. In terms of the mix of patients that we're seeing coming in, I think our trends would tell us that we continue to see an increase in the new to oxybate patients representing a larger portion, a growing portion of our of patients coming in at the top of the funnel through to Q3. Again, the largest portion in Q3 of patients starts were switch patients with the new to Oxybate, I would say closing the gap on the switch patient in terms of the percent mix. In terms of the dynamics of the switch, I'll maybe turn it over to Richard and 00:33:05.

Answer – Unidentified speaker: Yeah. As far as the switch patients are concerned, the majority are still coming from the mixed false patients overall here and we continue to see, expect that trend to continue. And as far as the marketplace, as far as the growth of OXYBATE, we don't have visibility on some of the twice-nightly sodium oxybate data at this point now, but we clearly see clear indicators But we could see some clear indicators that the overall narcolepsy market is growing. First we have the new to oxybate prescribers who have never written for twice-nightly oxybate around 150 of those now. We are seeing growth in the lower and moderate oxybate users, including patients who had previously wouldn't have been treated with the twice-nightly oxybate. And we also have the segment of patients who are previously discontinued on twice-nightly oxybates coming in LUMRYZ as well. And maybe the last treatment that we have for us is there's almost 20% of the HCPs that have written for LUMRYZ, that we either don't call on or have very minimal effort on. That's part of our plan with increasing our efforts to reach more of those providers. So we definitely see

opportunities to continue to build upon our foundation and continue to grow this market beyond where it has been with twice-nightly oxybates.

Answer – Unidentified speaker: Yeah, I think the only comment I would add, and maybe it's just putting a little bit of a different point on what Richard stated was there is no doubt since our launch we have added patients into the Oxybate pool that previously were not. Right and that's coming from both prescribers who have never written an oxybate and prescribers who wrote very minimal oxybate and are writing more. So by nature of that we believe Lumryz is adding new patients into the Oxybate pool. But to Richard's point, we don't have great visibility on what's happened with kind of the AG and Xyrem in that regard in terms of their volumes. But we feel confident we'll continue to expand those who are eligible and want to go on Lumryz.

Unidentified speaker

Question – Unidentified speaker: Thank you.

Answer – Unidentified speaker: Thanks Ami.

Operator

Thank you. We'll take our last question from David Amsellem with Piper Sandler. Your line is open.

Analyst:David Amsellem

Question – David Amsellem: Thanks. So couple from me. First, I don't know if you mentioned this earlier, but can you go through the mix between NT1 and and T2 for Lumryz and what you're seeing there? And then secondly, looking longer term, it looks like what we're seeing now is that the oxybate market is expanding. Your competitor continues to grow patients in the narcolepsy setting as well. So I guess the question is, as you think about the Orexin longer term, how are you thinking about the Oxybate footprint once it's in one Takeda and others coming to the market with their Orexin agonist several years from now? Thanks.

Answer – Unidentified speaker: Thanks, David. Richard, do you want to take those?

Answer – Unidentified speaker: Yeah. You know, David, as far as the mix of (00:36:10) what we see from prevalence is about 30% in (00:36:14) and what we see for Oxybate use, which has been consistent with LUMRYZ is about 70% use in Q1 and about 30% in Q2. So we would agree with you, as we just saw from the earlier question, we definitely see very solid signs that the oxybate market in narcolepsy is growing. And as far as the directions are concerned, you know, we have more to learn about their overall profile. You know, I think our view on it as we speak to thought leaders is they probably will have a, you know, an important impact on how we promote the agents for use. But our feedback that we see in general is a lot of the providers say a nice combination would really be an Orexin along with an oxybate and clearly there might having the taking away the need to sort of dosing middle night is important but to sort of be able to address with those daytime issues and potentially with those patients who may have challenges with their sleep or potentially insomnia as well, that that there's room for a growing marketplace and there's potentially room for an Orexin to be used along with an Oxybate in the future as well.

Answer – Unidentified speaker: Jen, anything you want to add to that?

Answer – Unidentified speaker: Sure.

sorry, again about the technical difficulties. So a couple of comments to add to what Richard said and specifically on the NT1, NT2 mix. We're really pleased that we're the only oxybate that has published data demonstrating consistent efficacy in both subgroups. This is certainly important based upon what Richard has said, where historically oxybate have been more reserved for narcolepsy type 1 and yet narcolepsy type 2 is the larger type of narcolepsy. In regard to the orexin agonist, we're certainly a company that is always going to recognize more options for patients are better. We continue to monitor the progress and of course, the focus with the orexin agonist as far as what is out in front is NT1 only and the focus is also on the daytime symptoms. So we have published data looking at the impact of LUMRYZ on the nighttime symptoms, specifically on disrupted nighttime sleep. And so, as Richard had mentioned, we continue to speak to leading KOLs who emphasize it, it's a matter of using both in the future and specifically LUMRYZ to avoid the middle of the night dose.

Unidentified speaker

Question – Unidentified speaker: Thanks, Jen and thanks, David. And again, apologize for the disruption technically.

Operator

Thank you. The question and answer session is now concluded. I will now turn the program back over to management for any additional or closing remarks.

Thank you, operator. Again, thank you, everyone for your time and joining us today for our third quarter 2024 earnings call. Have a great rest of your day and we look forward to catching up with you throughout the course of the next few days. Thanks.

Operator

That concludes today's teleconference. Thank you for your participation. You may now disconnect.

EXHIBIT 17

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UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT ----- JAZZ PHARMACEUTICALS, INC., and JAZZ PHARMACEUTICALS IRELAND LIMITED, Plaintiffs-Appellees, v. AVADEL CNS PHARMACEUTICALS, LLC, Defendant-Appellant. Nos. 24-2274, 24-2277, 24-2278 ----- PROCEEDINGS OF Oral Argument February 7, 2025 FINAL COPY JANE ROSE REPORTING 1-800-825-3341	1 (Beginning of Proceedings.) 2 THE COURT: The last case this morning is Jazz 3 Pharmaceuticals versus Avadel CNS Pharmaceuticals, 4 2024-2274, -77, and -78. Mr. Bell. 5 MR. BELL: Good morning, Your Honor. 6 THE COURT: Good morning. 7 MR. BELL: May it please the Court. Gabe 8 Bell for the appellant, Avadel. 9 The District Court's injunction in this case 10 goes directly to the heart of the safe harbor 11 protection that Congress provided precisely for 12 companies like Avadel that are developing, 13 investigating, and ultimately seeking approval for new 14 and unique treatments that can benefit the patients 15 and the public. 16 District Court's injunction even goes so far 17 as to prevent Avadel from seeking FDA approval. That 18 is the absolute core of what Congress wanted to 19 protect and encourage, especially here, where we have 20 a product that the FDA has deemed clinically superior 21 in a related context that's as to narcolepsy, and all 22 Avadel is trying to do here is allow FDA to make that 23 same, we believe, will be a readily apparent 24 conclusion for FDA in a different context, related 25 context of IH.
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APPEARANCES Appearing on behalf of Plaintiffs FRANK CALVOSA, ESQUIRE QUINN EMANUEL 51 Madison Avenue, 22nd Floor New York, NY 10010 Appearing on Behalf of Defendant GABRIEL BELL, ESQUIRE LATHAM & WATKINS 555 Eleventh Street, NW, Suite 1000 Washington, DC 20004 Panel Members Judge Alan Lourie Judge Jimmie Reyna Judge Richard Taranto JANE ROSE REPORTING 74 Fifth Avenue New York, New York 10011 1-800-825-3341 Wendy Sawyer, Transcriptionist	1 THE COURT: The safe harbor provision 2 applies with respect to non-infringing activity; is 3 that correct? 4 MR. BELL: It deems non-infringing 5 categories of activity that are about the regulatory 6 process. So developing and submitting information to 7 a regulatory body such as FDA for the purpose of, for 8 example, getting approval for a new treatment, that's 9 the core of the safe harbor provision. 10 And Congress further provided -- and this is 11 -- that was at subsection (e)(1). And in (e)(3), Congress 12 went so far as to say no injunction shall issue as to 13 conduct covered by Section (e)(1). Congress 14 anticipated that there would be these attempted end 15 runs to try to nonetheless stop the regulatory process 16 in its tracks before it can even get to FDA. 17 Congress, of course, had in mind rectifying 18 the twin aims at the front end of a patent term and at 19 the back end of the patent term. And it did so very 20 deliberately. It recognized that the regulatory 21 process can be involved. It can take some time. So 22 at the front end, the patentee shouldn't be penalized 23 for the regulatory process, initially, so you can 24 provide a patent term extension. That's in Section 25 156.

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1 THE COURT: The Court went through the four 2 factors with respect to an injunction. Do they really 3 matter? If you're presenting data to the FDA, isn't 4 that ipso facto exempted from infringement? 5 MR. BELL: Yes. It is, Your Honor. And 6 especially in this context where we're talking about 7 what's the proper scope of the remedy. So the 8 District Court had in front of it a request for an 9 injunction, and the safe harbor certainly plays into, 10 according to Congress in subsection (e)(3), what the 11 scope of that injunction can entail. 12 And if it cuts at activity that is even 13 reasonably related to seeking FDA approval or 14 reasonably related to submitting information, that is, 15 as a matter of law, as this court held in Classen, the 16 2015 version, as this Court held in Edwards, as this 17 court held in Abtox, as a matter of law, that conduct 18 is non-infringing. But here, we're even more 19 straightforward. 20 THE COURT: Well, infringing or non- 21 infringing would seem not to be the issue. If it's 22 non-infringing, the exemption doesn't really matter. 23 The exemption matters if there would otherwise be 24 infringement, and there would here because you've got 25 a composition claim which would dominate the use for	1 THE COURT: But I guess I was understanding 2 Judge Lourie's question to -- I don't want to ask. 3 Suppose you win here and you get to file -- do your 4 studies and get to file your application for the IH 5 indication on your drug, and the FDA says, I approve, 6 what's going to happen then on the assumption that you 7 have lost on the merits in this overall case? I don't 8 mean on this appeal. I mean, the overall case, what 9 you were just referring to. 10 MR. BELL: Sure. Absolutely, Your Honor. 11 THE COURT: The patent lasts till what, 12 2036? 13 MR. BELL: '36, I think thereabouts. That's 14 right. So a couple of things I would foresee 15 happening. If FDA is allowed to do its job, and if, 16 as we believe, it will find it clinically superior, 17 that would be a material change in the circumstances. 18 And we would go back to the District Court and say, 19 you should change the injunction to make this align 20 with your ruling in the narcolepsy context. 21 Would the District Court recognize that a 22 clinically superior drug that benefits patients 23 shouldn't be enjoined? So then we're in a very 24 different -- 25 THE COURT: I'm not sure it quite went that
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1 IH purposes. 2 MR. BELL: I think there would otherwise be 3 infringement as to the clinical studies at minimum. 4 But then the safe harbor kicks in and says it shall 5 not be infringing to conduct these trials. And I 6 don't think there's any meaningful dispute that the 7 Revitalize trial that Avadel is doing is precisely to 8 get FDA approval and a supplemental NDA for an 9 additional indication. And that aligns it exactly 10 with Classen, we submit. 11 THE COURT: Now, this patent's got a long 12 way to go, as I noticed. So either you've got to -- 13 if you get that approval, it's got to be held up, or 14 else you've got to prove the patent invalid. 15 MR. BELL: So it's a -- it's a good point, 16 Your Honor. And so I would take this opportunity to 17 note that -- 18 THE COURT: Most points from the Court are 19 presumed to be good. 20 MR. BELL: Thank you, Your Honor. And I do 21 so presume. And that leads me to point out the kind 22 of procedural quirk here where the District Court 23 decided to address the injunction before addressing 24 JMOLs on invalidity, which we expect to raise. I 25 probably would have done it in the reverse order.	1 far in the absence of generics -- 2 MR. BELL: Generics. 3 THE COURT: -- (inaudible). 4 MR. BELL: And there's -- and the litigation 5 ongoing. We don't know what the landscape will look 6 like two years from now. 7 THE COURT: Let's assume all of that away. 8 MR. BELL: Well, at the end of the day, 9 if -- 10 THE COURT: Let's suppose, as I think the 11 other side has suggested, that, in fact, superiority 12 over your product may well not be decided by the FDA, 13 may not be necessary for FDA approval. FDA approval 14 and your comparative study may not be in fact 15 doing the comparison. 16 So just assume that the FDA approves the 17 drug and the IH use of their, what, Xywav drug is not 18 yet met with any competition, do you then -- if you're 19 then, what, barred by this injunction in the absence 20 of a Rule 60 type ground for change of circumstances 21 for getting relief from it? 22 MR. BELL: In the absence of that or in the 23 absence of a subsequent appeal that would show the 24 patent to be invalid, right, that's the other thing 25 that's coming down the pipe eventually.

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1 And so I suppose if we lose all of those, 2 then, yes, the injunction would still stand. That 3 would lead me, though, to our second basis for 4 challenging the injunction was that the eBay factors 5 themselves were improperly weighted in the sense of 6 looking at harm that's speculative. 7 In Monsanto, the Supreme Court said it has 8 to be imminent. And they relied not on anything 9 imminent. They relied on the possibility of 10 marketing, which was at least two years away. And all 11 these things could happen in the meantime. I mean, 12 generics could come on the market. 13 There could be a clinical superiority 14 finding by the FDA. It doesn't make sense, we argued 15 to the District Court and argue here, to do that in a 16 vacuum weighing the eBay factors. 17 Now, of course, our primary argument is at 18 the very bare minimum, the scheme that Congress put in 19 place in 1984 requires the regulatory process to at 20 least come up to the point of being approved. And 21 then you deal with the patent stuff, the consequences 22 after that. That's what the HR report said that 23 accompanied the bill. 24 THE COURT: So for the application that you 25 want to submit for the IH indication on --	1 the patent that they're asserting. They don't have an 2 extended release version. 3 That's what Avadel came up with. That's 4 what Jazz couldn't do. That's why Avadel's product is 5 clinically superior for narcolepsy because you can 6 take an extended release dose that lasts over time, 7 and you can take a higher dose. You can go up to nine 8 grams, whereas theirs is limited to six grams and 9 immediate release. 10 And, you know, just speaking as somebody 11 who's had medications that are immediate release and 12 extended release, that can make a very meaningful 13 difference in your life. 14 And that was shown to be true in the 15 narcolepsy context. And we think it will equally be 16 shown true in the IH context. And all they're asking 17 is to allow FDA to do its job as Congress intended. 18 THE COURT: Can I ask you a question? Why 19 doesn't your stipulation to infringement, which is 20 quite broadly worded, prevent you from relying on 21 (e)(1) here? 22 MR. BELL: So the stipulation says pursuant 23 to 271(a). That's how it reads. And so our position 24 is we didn't mean to convert per se non-infringing 25 conduct into infringing conduct. 271(a) itself says
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1 MR. BELL: Yes. 2 THE COURT: -- what is it? 3 MR. BELL: Lumryz. 4 THE COURT: Lumryz? 5 MR. BELL: Lumryz. Correct. Yes, Your 6 Honor. Correct. 7 THE COURT: Okay. That would not come with 8 a 30-month automatic stay? 9 MR. BELL: No. 10 THE COURT: It would not. 11 MR. BELL: No. 12 THE COURT: So if the injunction is lifted 13 for the application to -- for that approval and you 14 get the approval, will there then be a new application 15 for preliminary injunction by Jazz and you'll have to 16 litigate that under -- 17 MR. BELL: Yes. 18 THE COURT: -- extremely rushed 19 circumstances? 20 MR. BELL: I mean, I would assume that. 21 They've shown propensity to do that. I would assume 22 they would do that in this case. And the point I'd 23 like to make there is the reason we're not dealing 24 with an automatic stay is we're not dealing with an 25 Orange Book listed patent here. Jazz doesn't practice	1 except as otherwise provided in this section, comma -- 2 THE COURT: Right. But your stipulation was 3 that your activities infringe under 271(a). 4 MR. BELL: Well, I think in the context of 5 the case -- 6 THE COURT: It may have been unfortunately 7 worded, but it didn't make an exception for the 8 exception to 271(a). 9 MR. BELL: Well, our position is that it's 10 implicitly there. If you cut and paste the 271(a) 11 language in there, we're stipulating that under this 12 provision, the whole thing, not part of it, we 13 infringe, meaning, still subject, of course, to things 14 like submitting paperwork to the FDA, which I don't 15 think frankly is even a use of a drug to begin with. 16 Right? 17 So if you want to talk about the actual 18 language of 271(a) -- make, use, import, etcetera -- 19 simply submitting papers, like submitting papers to 20 this Court about this patent invention, that's not a 21 use of it. Right? Submitting information in a 22 database isn't use of a drug as this Court held in the 23 last iteration of this. 24 THE COURT: But would it also be the case 25 that use is specifically addressed by 271(e)(2) for

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1 which very well defined remedies are specified in the 2 statute, and those remedies do not include this kind 3 of injunction? 4 MR. BELL: Absolutely. So even -- let's 5 presume it was an Orange Book listed patent, which is 6 what (e)(2) goes to. 7 THE COURT: Yes. 8 MR. BELL: The Supreme -- It's not in the 9 text necessarily, but the Supreme Court has read it to 10 be related. 11 THE COURT: And you're not that. You're a 12 505(b)(2). 13 MR. BELL: We're not that. There's no 14 Orange Book listed patent. There's no paragraph four 15 certification that would trigger (e)(2) infringement, 16 but let's even assume there was. The Court is 17 absolutely right. There are four and only four 18 remedies that you can get even for that artificial act 19 of infringement. And not one of those is enjoining 20 the submission to FDA. 21 You could delay FDA approval, right, if 22 there's an Orange Book, that's not what we're dealing 23 with here, but the others all relate to damages and 24 non-injunctive relief. 25 And in (c)(3), the Congress couldn't have been	1 where Avadel does not dispute that it claims it will 2 make billions of dollars. 3 What the injunction does is it very 4 limitedly says Avadel can't expand that infringement 5 even further. And it focuses on the IH market where 6 Jazz already has an FDA-approved safe and effective 7 once nightly drug for the treatment of IH. That was a 8 distinguishing factor in narcolepsy. Jazz only had 9 twice nightly. 10 The District Court found based on clinical 11 research and competing expert declarations that there 12 was factual evidence amid factual findings that Jazz's 13 once-nightly dosage is not substantially different 14 than its twice-nightly dosage in IH. 15 THE COURT: Can I just ask so I -- 16 MR. CALVOSA: Yes, Your Honor? 17 THE COURT: On the irreparable harm part of 18 the District Court's analysis with respect to the IH 19 use, my recollection is that the District Court said 20 that if IH is marketed, then there's going to be 21 irreparable harm to Jazz. But it didn't ever make a 22 finding that the specifically enjoined activities here 23 that are at issue on appeal, namely asking for 24 approval from the FDA, conducting clinical studies to 25 get that approval, and, what, allowing the patients in
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1 more clear. No injunctive relief shall issue for safe 2 harbor activities. We think that's the start and the 3 end of this case. And with that, I'll reserve my 4 rebuttal time. 5 THE COURT: We will save it for you. 6 MR. BELL: Thank you. 7 THE COURT: Mr. Calvosa. 8 MR. CALVOSA: Good morning, and may it 9 please the Court. Frank Calvosa from Quinn Emanuel 10 Urquhart & Sullivan on behalf of Jazz Pharmaceuticals. 11 The District Court used its discretion to carefully 12 craft the limited injunction in this case. 13 The patent that's at issue has already been 14 tried. Avadel stipulated to infringement. Avadel 15 failed to succeed on its invalidity defenses. With 16 respect to the -- 17 THE COURT: So far. 18 MR. CALVOSA: So far. I think -- great. I 19 believe it will continue in the future. 20 With respect to the injunction, Avadel 21 already has its infringing products commercially 22 available on the market, which makes this unlike other 23 cases where the safe harbor is at issue. And under 24 the injunction, Avadel is permitted to continue and 25 expand upon its infringement in the narcolepsy market,	1 the 150-person study to continue the 18 or 20 weeks or 2 something for the open label extension, that those 3 would cause irreparable harm to your client. Is there 4 a crucial missing element? 5 MR. CALVOSA: A couple of things, Your 6 Honor, is, first of all, Avadel did not raise the safe 7 harbor argument below. It did not raise the open 8 label extension argument below until the stay briefing 9 before the District Court. Avadel had full view of 10 the injunction that Jazz was seeking and raised none 11 of these arguments during injunction briefing. And 12 then they seek to fault the District Court for not 13 addressing it. 14 I want to circle back to the OEL at the end 15 because the District Court did speak to that in 16 denying Avadel's stay request. But the -- evidence 17 was before the District Court that harm is already 18 taking place. Avadel is on the market approved for 19 narcolepsy, but the product is also being used already 20 for IH. 21 They have an infringing sales in IH. And 22 another portion of the injunction is that Avadel 23 cannot make, use, or sell, or market in any condition 24 other than narcolepsy, and that includes IH. 25 THE COURT: If it's being used -- it's on

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1 the market for narcolepsy now. If it's being used for 2 IH, that's sort of off label. But if they're 3 seeking -- if they're seeking approval by the FDA for 4 IH, that's exempted from infringement by statute. 5 MR. CALVOSA: And that's another point that 6 I lost in what I'm saying. In the modified 7 injunction, the clarified injunction -- in the 8 clarified injunction, and this is at Appendix 41, the 9 District Court says, Avadel, you could do your 10 Revitalize trial. Avadel, you could submit that 11 information and results to the FDA. 12 What is enjoined, and this is very 13 important, is not the submission of an application to 14 the FDA. It's seeking approval until the patent 15 expires. The safe harbor does not protect FDA 16 approval as of any certain date. It doesn't mean 17 Avadel has to get approval now. Avadel is free to 18 submit their application, but with that, they would 19 have to tell the FDA, we are not seeking approval 20 until February 18, 2036. That's what the injunction 21 says. 22 Avadel's free to submit their application. 23 They're free to submit information in support of 24 clinical superiority. We don't think they're going to 25 get it. We already have a --	1 current injunction from marketing, and that gets lost 2 in the argument as well. The current injunction 3 enjoins make, use, or sell marketing in addition to 4 the seeking FDA approval until a certain date. 5 And when an applicant goes to the FDA, they 6 say I'm seeking approval as of before expiration of 7 patents, as of expiration of patents at this date. 8 The applicant can specify in their submission which 9 date they're doing. 10 THE COURT: Let me just see if I understand 11 this. So -- 12 MR. CALVOSA: Yes, Your Honor. 13 THE COURT: Not challenged here is the part 14 of the injunction that prevents -- prohibits Avadel 15 from marketing for IH use. 16 MR. CALVOSA: Avadel challenges that only on 17 the public interest factor. That's the only challenge 18 they make to the eBay for the make, use, or sell, as I 19 understand it. So when my friend said that if they 20 were to get approval -- 21 THE COURT: Put that -- put that -- 22 MR. CALVOSA: Sure. 23 THE COURT: Assuming that that is not at 24 issue, then the only things that are the issue are 25 activities leading to FDA approval or a request for
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1 THE COURT: The injunction says they're not 2 free to submit it. 3 MR. CALVOSA: This is at Appendix 41, Your 4 Honor. It says, finally, while the order enjoins 5 Avadel from seeking FDA approval for IH, the order does 6 not enjoin Avadel from submitting information or 7 results from ongoing clinical studies to the FDA, and 8 Avadel's permitted to continue the Revitalize trial. 9 And the injunction at Appendix 36 10 specifically says that Jazz's motion for a limited 11 permanent injunction prohibiting Avadel from seeking 12 approval from the US Food and Drug Administration and 13 marketing Lumryz is granted, but it's only through the 14 expiration of the '782 patent. 15 So Avadel is allowed to submit that 16 application. They can't seek approval until February 17 of 2036. They're enjoined from doing so. This is no 18 different than any other application that somebody 19 submits to the FDA. 20 THE COURT: Well, they can seek approval, 21 but they can't act on it. 22 MR. CALVOSA: Well, no. When you -- 23 THE COURT: If they acted on it by 24 marketing, they're at risk. 25 MR. CALVOSA: They're enjoined under the	1 FDA approval, right? 2 MR. CALVOSA: Somewhat, yes. 3 THE COURT: Get FDA approval, assuming the 4 injunction -- I'm going to assume it bars sale and 5 marketing -- they can't actually jump into the market. 6 MR. CALVOSA: Well, here's the issue, and 7 this is what the District Court foresaw, is that 8 because they are already on the market and the product 9 is out there, what happens is with FDA approval, and 10 Avadel doesn't dispute this, FDA posts the labeling on 11 the website. 12 Pursuant to FDA regulations, Avadel must 13 then use that labeling with the IH indication out 14 there when it disseminates its product. This Court 15 has been clear, on indication use in a label is 16 infringement. It's certainly marketing that's barred 17 under the injunction. 18 Here, because this isn't an Orange Book 19 patent, the District Court cannot enjoin the FDA from 20 approving the drug. 21 The District Court cannot enjoin the FDA 22 from posting that label on the website or requiring 23 Avadel to use it. What the District Court could and 24 did do was enjoin Avadel from asking for FDA approval 25 until a certain date, which is what applicants can and

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1 do do all the time. 2 THE COURT: Let me see if I understand. If 3 the FDA were to approve, the District Court would have 4 to face the question whether this injunction precludes 5 Avadel when selling this product from using a label 6 that the Food and Drug Act would require it to use? 7 MR. CALVOSA: No. The District Court's 8 injunction already precludes an infringing use, and it 9 would be on the label at that point in time. The way 10 this works in other cases, if there's -- 11 THE COURT: I don't think I'm communicating 12 because I didn't hear that as an answer to my 13 question. 14 MR. CALVOSA: Okay. I apologize. 15 THE COURT: I'm trying to get very concrete 16 about what is the problem with allowing the FDA 17 approval process to go forward now. 18 MR. CALVOSA: The problem with that is that 19 we'll be right back in front of the District Court if 20 Avadel were to get approval, because then they'd have 21 to have that new labeling out there, and the District 22 Court's injunction bars make-use-sell marketing. That 23 new -- 24 THE COURT: So I would -- I guess I'm taking 25 as a premise for purposes of this question that	1 can't seek approval until a certain date. 2 So you file your application, you say you're 3 enjoined -- we're enjoined from getting approval until 4 February 2036. 5 THE COURT: Could the FDA grant approval 6 even if Avadel simply refrains from asking it to grant 7 the approval? Because you're now saying it could file 8 its application. 9 MR. CALVOSA: Yes. Avadel could do that. 10 Our position is that the FDA would not grant approval 11 in that case, and that's what applicants -- 12 THE COURT: Couldn't or just wouldn't? 13 MR. CALVOSA: Or just wouldn't. That's what 14 applicants do all the time. If they file an 15 application, they could say, I'd like approval before 16 a patent expires. I would like approval when a patent 17 expires. This is not -- this is not an injunction on 18 seeking FDA approval in a vacuum, full stop, as Avadel 19 tries to make it seem. It's tied to a specific date 20 because they've already been adjudicated infringers of 21 that patent. 22 THE COURT: And so there's the approval 23 request issue, there's the OLE issue, and there's the 24 doing more clinical studies issue. 25 MR. CALVOSA: For the OLE and the doing more
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1 offering the product with a label that identifies IH 2 use would, in fact, be marketing contrary to the 3 current injunction. 4 MR. CALVOSA: Exactly. And then Jazz would 5 be right back in front of the District Court for a 6 contempt proceeding because they would -- Avadel would 7 be marketing. And the District Court foresaw this. 8 And the District Court made factual findings that 9 entering the market for IH would irreparably harm 10 Jazz's exclusivity there. And Avadel had already had 11 off label sales. And Avadel's excuse was, well, we 12 don't promote it. And that is at Appendix 9069. 13 And they also say that in their briefing 14 before the District Court at Appendix 7510, because we 15 don't have the labeling, we don't promote. But with 16 FDA approval comes that labeling. I know that this 17 Court's case law, Braintree, GSK v. Teva, if you have 18 an on use indication label, that's inducing 19 infringement. 20 So the District Court said you could submit 21 your information, Avadel, and we don't dispute that. 22 They could file their application. They could submit 23 information. They could go back and forth with the 24 FDA. What they need to tell the FDA and what the 25 District Court's injunction says is we can't -- you	1 clinical studies, there is no record evidence below 2 that that activity falls within the safe harbor. You 3 have to look under this Court's case law on the 4 Supreme Court -- 5 THE COURT: Doing clinical tests 6 necessarily, they don't -- they don't do it for 7 academic reasons. They want to get approval to sell a 8 product. 9 MR. CALVOSA: Well, the District Court made 10 a factual finding at Appendix 43 that these OLE trials 11 are marketing activities dressed up as research. It 12 quoted from a paper that Jazz put in during the stay 13 briefing. And if it's solely for -- 14 THE COURT: At least in my mind, I think of 15 there being two questions. One is new clinical 16 trials. Second is the OLE extensions. Can you put 17 aside the OLE extensions for a moment? 18 MR. CALVOSA: Yes, Your Honor, I can. 19 THE COURT: Just new clinical trials, how 20 could it possibly be that a new clinical trial would 21 not be within the (e)(1) exemption? 22 MR. CALVOSA: Because under both Supreme 23 Court case law and this Court's case law, you have to 24 look at each and every use. And it is a factual 25 question. We saw in Amgen v. ITC and even

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1 Hospira -- sorry. 2 THE COURT: What if the injunction were 3 modified to say, the injunction does not preclude 4 clinical trials covered by (e)(1), but we actually 5 have one that we already know enough about, so we're 6 going to get concrete about the only current one on 7 the table and say that that's in or out? But there's 8 a general -- there would be a general carve out for 9 (e)(1) -- 10 MR. CALVOSA: I think what the proper remedy 11 here would be is that if Avadel has, under this 12 Court's case law, reasonable, necessary clinical 13 trial, each and every use they would have to prove 14 Rule 60(b) provides for a modification. And Avadel 15 could go back to the District Court. They could even 16 come to Jazz beforehand and say, hey, the FDA told us 17 we need to do this study. And the parties could deal 18 with it then, but -- 19 THE COURT: You say they're doing these new 20 clinical trials for marketing purposes, but don't 21 those data still have to be presented to the FDA? 22 MR. CALVOSA: No, Your Honor. They don't. 23 And for example, the OLE in the Stern declaration, 24 that's ECF 23, Exhibit 2, page 59 to 60, for example, 25 says the OLE is completely voluntary. It's not a	1 THE COURT: Okay. 2 MR. CALVOSA: Every use of the drug would be 3 safety information then. And under FDA requirements, 4 once you get approval, you're required to put in 5 adverse events in safety information. This is routine 6 use, which under Momenta 2, the 2015 decision, isn't 7 covered by safe harbor. The parties didn't get to 8 litigate that because Avadel didn't raise it. 9 And to the extent that the District Court 10 did address it, it rejected the OLE at Appendix 43. I 11 see I'm out of time. I'm happy to answer any other 12 questions, but we believe the District Court's 13 decision should be upheld. 14 THE COURT: Thank you, counsel. 15 MR. CALVOSA: Thank you, Your Honor. 16 THE COURT: Mr. Bell has some rebuttal time. 17 MR. BELL: Thank you, Your Honor. I think 18 what's clear now is what we're really talking about 19 here is a de facto patent term extension. They want 20 to muck up the regulatory process that Congress 21 allowed for in the safe harbor and start to parse it 22 out and say, you can do this part or you can do that 23 part, but you can't do all of the things that are 24 reasonably related. Right? 25 So, you can't -- you can submit an
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1 requirement that the FDA put in place for that 2 protocol. 3 And even at page 9 of that exhibit to the 4 Stern declaration, that's Exhibit 2 to the Stern 5 declaration, which was ECF 23, it explains that the 6 only efficacy information and patient population for 7 the study is coming from the Revitalize trial, not 8 the open label extension. And in this case where 9 Avadel is already on the market, unlike other cases -- 10 THE COURT: Isn't there -- I don't remember 11 whether it's an assertion by Avadel's lawyers or 12 something in the evidence that the use for the extra 13 number of weeks when the patient that had been in the 14 trial after the endpoint and now has -- it's open 15 label, so the patient knows I'm getting the good stuff 16 and not the placebo or something, uses it, that that 17 actually would be safety-related information. 18 MR. CALVOSA: If you take that then every -- 19 THE COURT: Is that -- I mean -- 20 MR. CALVOSA: They made that argument. The 21 District Court didn't credit it. And furthermore -- 22 THE COURT: Was there evidentiary support 23 for that argument or is this just -- 24 MR. CALVOSA: This was an argument that they 25 made that it includes safety information.	1 application, but you can't ask for FDA approval. I'm 2 not sure I totally understand that. What Congress 3 said is that you can't enjoin safe harbor conduct, and 4 that includes submitting for and asking for FDA 5 approval. I think that is squarely within the safe 6 harbor. 7 Clinical trials leading up to it, as Your 8 Honor noted, we don't do them -- 9 THE COURT: I'm sorry to -- 10 MR. BELL: Yes. 11 THE COURT: -- interrupt. Why is asking for 12 FDA approval within the language of (e)(1)? 13 MR. BELL: It's within the language of 14 (e)(1), which provides for -- 15 THE COURT: Asking for it -- I'm going to 16 assume that that is not actually infringing under 17 271(a), but that's not the point you're making here. 18 MR. BELL: Oh, if we assume it's not even 19 infringing under 271(a), then you don't need the safe 20 harbor for it. I think that would be kind of the 21 first line. Right. It's not actually a use. 22 THE COURT: So go -- tell me about (e)(1). 23 MR. BELL: Sure. So (e)(1) says, use is 24 reasonably related to the development and submission 25 of information under a federal law. And the whole

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1 point of this was this court in Roche had said that 2 you can deem those regulatory activities for seeking 3 approval as kind of de facto marketing. That's the 4 position Jazz wants to take now. And Congress 5 resoundingly said, no, we're going to let the 6 regulatory process play out. 7 And so for -- in Classen, for example, this 8 court in 2015, very similar facts. There was an 9 already approved drug. The party realized that there 10 was a different interaction with food. It did 11 voluntary, this Court said, voluntary studies to 12 determine that interaction and then put that 13 interaction on the label via a supplemental NDA, SNDA 14 clinical studies, a supplemental NDA seeking FDA 15 approval. 16 This Court said that was "clearly" -- all of 17 that was "clearly within the safe harbor" and ruled as 18 a matter of law on summary judgment. 19 THE COURT: What's your response to the 20 other side's argument that you waived -- you waived 21 your safe harbor argument? 22 MR. BELL: Yeah. So a couple of things, 23 Your Honor, and I see I'm getting close on time. This 24 is really about the scope of the injunctive relief. 25 So, we have the liability phase, which led up to the	1 something? 2 MR. BELL: Yes, of course, Your Honor. 3 THE COURT: So on the assumption that a part 4 of the injunction not having to do with the FDA, that 5 just you cannot market, let's call it that. 6 MR. BELL: Right. 7 THE COURT: If you go ahead and you get FDA 8 approval, at that point you're actually barred from 9 marketing, from acting on the FDA approval to market. 10 I think the other side said that at that -- once 11 there's FDA approval, your label has to include the 12 indication, which I'm going to assume for purposes of 13 this question is marketing. What's supposed to 14 happen? 15 MR. BELL: Well, I think, according to my 16 friend, we'd end up back in front of District Court, 17 and we would sort it out there, what's the appropriate 18 path going forward. Right. And so that's appropriate 19 because Congress has kind of said what happens up 20 until then. Congress says you have to allow this 21 process to play out and not just for the benefit of 22 the party seeking it. It's for the benefit of the 23 patients, and it's for the benefit of the public as 24 well. 25 THE COURT: Would the District Court have
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1 injunctive proceedings, and then it's the scope of the 2 injunction that's at issue. And squarely raised at 3 least a half a dozen times at the hearing was the 4 statutory safe harbor. And in fact, at one point, the 5 District Court, and this is at a -- 6 THE COURT: But just to be clear, not in 7 your actual papers. 8 MR. BELL: Correct. It was not in the 9 brief. We presumed at a couple points that we would 10 be allowed to, but didn't come out and say safe 11 harbor. But it was teed up squarely at the hearing 12 and the District Court said, "Right, that's protected 13 by statute." 14 And when the other side was pressed on it, 15 they didn't say there was any sort of waiver, either 16 during the hearing, in fact, after the hearing in 17 response to our letter, they said, we never contended 18 that you couldn't do trials. And thereafter, the 19 District Court didn't find a waiver in considering the 20 issues on the stay motion where they raised waiver. 21 This Court didn't find it in granting a 22 partial stay. We think the safe harbor was clearly 23 raised, and we've cited in our brief six different 24 places at the hearing. 25 THE COURT: Can I just come back to	1 the authority at that point? Suppose the District 2 Court concludes, really would be irreparable harm. 3 The FDA hasn't indicate- -- hasn't said that your 4 product is superior in a meaningful way. And so in 5 ordinary, eBay injunction terms, an injunction is 6 warranted, would the District Court be able to 7 authorize to keep that injunction in place, 8 notwithstanding the FDA approval? 9 MR. BELL: I think we would have to litigate 10 it. I think we absolutely would have to litigate it. 11 And I think an important point here is my friend said 12 there would be induced infringement, putting it on the 13 label. 14 Notably here, they asserted induced 15 infringement initially, but that's not what the 16 stipulation addresses. Stipulation addresses direct 17 infringement. So we're in a world where the direct 18 infringement is enjoined for marketing, not induced 19 infringement. 20 THE COURT: Didn't the Court account for all 21 this by limiting the injunction? 22 MR. BELL: They did not limit it enough, 23 Your Honor. The injunction specifically says -- and 24 this is Appendix page 36 -- 25 THE COURT: But enough to recognize your

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arguments or the position that you're taking now.
MR. BELL: Well, I think it at the hearing seemed to recognize our arguments and saying that's protected by statute, but then ultimately in the actual injunction prohibited seeking FDA approval, which simply is irreconcilable with the scheme that Congress put out, particularly in Section (e)(3), which says no injunction shall issue on safe harbor conduct.

And we think that disposes of this case for the benefit of the patients and the public. Avadel should be able to seek FDA approval for IH, for other indications that may come. Sleep disorders are a terrible thing for the people suffering from it. And those patients shouldn't have to suffer.

Avadel has a superior product in narcolepsy. We think the same will be true in IH. For that reason, the injunction should be rejected.

THE COURT: We've heard your argument. There's no narcolepsy here.

MR. BELL: Thank you, Your Honor.

THE COURT: The case is submitted, and that concludes today's argument.

(End of Proceedings.)

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CERTIFICATE OF TRANSCRIPTION

Jane Rose Reporting does hereby certify that the foregoing transcript is a true and correct record of the recorded proceedings; that said proceedings was transcribed to the best of our ability from the audio receiving; and that Jane Rose Reporting is neither counsel for, nor related to, any of the parties to this case, and have no interest, financial or otherwise, in its outcome.

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EXHIBIT 18

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-K

(Mark One)

☒ ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2024

or

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission File Number: 001-33500

JAZZ PHARMACEUTICALS PUBLIC LIMITED COMPANY

(Exact name of registrant as specified in its charter)

Ireland

(State or other jurisdiction of incorporation or organization)

98-1032470

(I.R.S. Employer Identification No.)

Fifth Floor, Waterloo Exchange

Waterloo Road, Dublin 4, Ireland D04 E5W7

011-353-1-634-7800

(Address, including zip code, and telephone number, including area code, of registrant’s principal executive offices)

Securities registered pursuant to Section 12(b) of the Act:		
Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary shares, nominal value \$0.0001 per share	JAZZ	The Nasdaq Stock Market LLC
Securities registered pursuant to Section 12(g) of the Act:		
None		

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of “large accelerated filer,” “accelerated filer,” “smaller reporting company,” and “emerging growth company” in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐ Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management’s assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant’s executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant, as of June 28, 2024, the last business day of the registrant’s most recently completed second fiscal quarter, was approximately \$6,413,308,100 based upon the last sale price reported for the registrant’s ordinary shares on such date on The Nasdaq Global Select Market. The calculation of the aggregate market value of voting and non-voting common equity excludes 1,655,566 ordinary shares of the registrant held by executive officers, directors and shareholders that the registrant concluded were affiliates of the registrant on that date. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

As of February 19, 2025, a total of 60,732,479 ordinary shares, nominal value \$0.0001 per share, of the registrant were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III, Items 10-14 of this Form 10-K is incorporated by reference to the registrant’s definitive Proxy Statement for the 2025 Annual General Meeting of Shareholders to be filed with the Securities and Exchange Commission pursuant to Regulation 14A. If such Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Form 10-K, such information will be included in an amendment to this Form 10-K to be filed within such 120-day period.

JAZZ PHARMACEUTICALS PLC
40134
2024 ANNUAL REPORT ON FORM 10-K

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Defined Terms and Products
Defined terms

We use several terms in this Form 10-K, including but not limited to those that are finance, regulation and disease-state related as well as names of other companies, which are given below.

Term	Description
2007 Directors Award Plan	2007 Non-Employee Directors Stock Award Plan
2011 Plan	2011 Equity Incentive Plan
2015 Credit Agreement	Credit agreement dated as of June 18, 2015 (as amended) among Jazz Pharmaceuticals plc, and certain of our other subsidiaries as borrowers, the lenders party thereto and Bank of America, N.A., as administrative agent and collateral agent
2024 Notes	1.50% exchangeable senior notes due 2024
2025 Proxy Statement	definitive proxy statement for our 2025 annual general meeting of shareholders
2026 Notes	2.00% exchangeable senior notes due 2026
2030 Notes	3.125% exchangeable senior notes due 2030
340B program	U.S. Public Health Service's 340B program
ADR	administrative dispute resolution
ADS	American Depositary Shares
Aetna	Aetna Inc.
AFL Plan Lawsuit	On July 31, 2020, a class action lawsuit was filed in the United States District Court for the Southern District of New York by the A.F. of L.-A.G.C. Building Trades Welfare Plan on behalf of itself and all others similarly situated, against Jazz Pharmaceuticals plc
AG	authorized generic
AI	artificial intelligence
Alkem	Alkem Laboratories Ltd.
ALL	acute lymphoblastic leukemia
Amended Credit Agreement	Credit Agreement amended to include the Repricing Amendment No. 1, the Repricing Amendment No. 2 and Amendment No. 3
Amended Revolving Credit Facility	Revolving credit facility amended to increase the Initial Revolving Credit Facility to \$885.0 million and extend the maturity date
Amended Revolving Facility Maturity Date	November 26, 2029
Amendment No. 3	amendment to the Credit Agreement entered into by Jazz Lux in November 2024
AML	acute myeloid leukemia
Amneal	Amneal Pharmaceuticals LLC
ANDA	abbreviated new drug application
API	active pharmaceutical ingredient
Ascent	Ascent Pharmaceuticals, Inc.
ASD	ASD Specialty Healthcare LLC
ASP	average sales price
ASU	Accounting Standards Update
Audit Committee	audit committee of our board of directors
Autifony	Autifony Therapeutics Limited
Avadel	Avadel Pharmaceuticals plc
Axsome	Axsome Therapeutics, Inc.
Azur Merger	the merger of Jazz Pharmaceuticals, Inc. and Azur Pharma in January 2012
Azur Pharma	Azur Pharma Public Limited Company
BCBS	Blue Cross and Blue Shield Association
BCBS Defendants	Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA), Inc., Hikma Pharmaceuticals plc, Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals Inc., and Lupin Inc.

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Term	Description
BCBS Lawsuit	On June 17, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by BCBS against Company Defendants
Biophore	Biophore Pharma, Inc. and Zenara Pharma Private Ltd.
BLA	Biologics License Application
BPCIA	Biologics Price Competition and Innovation Act
BTC	biliary tract cancers
Cardinal	Cardinal Health, Inc.
CAT	Irish capital acquisitions tax
CBD	cannabidiol
Cencora	Cencora, Inc. (formerly named AmerisourceBergen Corporation)
cGMP	current Good Manufacturing Practices
CIO	Chief Information Officer
CISO	Chief Information Security Officer
City of Providence Defendants	Jazz Pharmaceuticals plc, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Hikma Labs Inc., Hikma Pharmaceuticals USA Inc., and Hikma Pharmaceuticals plc
Clinigen	Clinigen Group plc
CMS	U.S. Centers for Medicare & Medicaid Services
Code	U.S. Internal Revenue Code
CODM	chief operating decision maker
COG	Children's Oncology Group
Company Defendants	Jazz Pharmaceuticals plc, Jazz Pharmaceuticals, Inc., and Jazz Pharmaceuticals Ireland Limited
ConcERTos	Employee Resource Teams
COSO framework	Committee of Sponsoring Organizations of the Treadway Commission Internal Control - Integrated Framework (2013)
CREATES	Creating and Restoring Equal Access To Equivalent Samples Act
Credit Agreement	Credit Agreement entered into on May 5, 2021, by and among us, Jazz Lux, and certain of our other subsidiaries, as borrowers, the lenders and issuing banks from time to time party thereto, Bank of America, N.A., as administrative agent and U.S. Bank Trust Company, National Association, as collateral trustee
CSA	Federal Controlled Substances Act
DDI	drug-drug interaction
DEA	U.S. Drug Enforcement Administration
Defendants	Express Scripts, Inc., Express Scripts Holding Company, Express Scripts Specialty Distribution Services, Inc., Curascript, Inc. d/b/a Curascript, S.D., Priority Healthcare Distribution, Inc. d/b/a Curascript SD and Curascript Specialty Distribution SD, Caring Voice Coalition, and Adira Foundation (collectively with the Company Defendants)
DEI	diversity, equity and inclusion
DOJ	U.S. Department of Justice
Dollar Term Loan	our former seven-year \$3.1 billion term loan B facility under the Credit Agreement
DS	Dravet syndrome
DTC	Depository Trust Company
EC	European Commission
EDS	excessive daytime sleepiness
EEA	European Economic Area
EMA	European Medicines Agency
Epidiolex ANDA Filers	Teva Pharmaceuticals, Inc.; Padagis US LLC; Apotex Inc.; API Pharma Tech LLC and InvaGen Pharmaceuticals, Inc.; Lupin Limited; Taro Pharmaceutical Industries Ltd.; Zenara Pharma Private Limited and Biophore Pharma, Inc.; MSN Laboratories Pvt. Ltd. and MSN Pharmaceuticals, Inc.; Alkem Laboratories Ltd.; and Ascent Pharmaceuticals, Inc.
Epidiolex Patent Litigation	On January 3, 2023, we filed a patent infringement suit against the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey.
ESPP	employee stock purchase plan
ESSDS	Express Scripts Specialty Distribution Services, Inc.

Term	Description
ET	essential tremor
ETASU	elements to assure safe use
EU	European Union
EURIBOR	Euro Inter-Bank Offered Rate
Euro Term Loan	our now repaid seven-year €625.0 million term loan B facility under the Credit Agreement
Exchange Act	Securities Exchange Act of 1934, as amended
Exchangeable Senior Notes	our 2026 Notes and 2030 Notes
Fair value step-up expense	the acquisition accounting inventory fair value step-up expense
FASB	Financial Accounting Standards Board
FCP	Federal Ceiling Price
FCPA	U.S. Foreign Corrupt Practices Act
FDA	U.S. Food and Drug Administration
FDCA	Federal Food, Drug, and Cosmetic Act
FSS	Federal Supply Schedule pricing program
FTC	Federal Trade Commission
GDPR	EU's General Data Protection Regulation
GEA	gastroesophageal adenocarcinoma
GEHA Lawsuit	Class action lawsuits filed on June 23, 2020 against the Company Defendants and the BCBS Defendants by Government Employees Health Association Inc. in the United States District Court for the Northern District of Illinois
GHB	gamma-hydroxybutyric acid
GMP	Good Manufacturing Practice
GW	GW Pharmaceuticals plc
GW Acquisition	our acquisition of GW Pharmaceuticals plc in May 2021
GW Incentive Plans	GW Pharmaceuticals plc 2008 Long-Term Incentive Plan, GW Pharmaceuticals plc 2017 Long-Term Incentive Plan and GW Pharmaceuticals plc 2020 Long-Term Incentive Plan, each as amended from time to time
Hatch-Waxman Act	Drug Price Competition and Patent Term Restoration Act of 1984
HHS	U.S. Department of Health and Human Services
Hikma	Hikma Pharmaceuticals PLC
HIPAA	Health Insurance Portability and Accountability Act of 1996 and its implementing regulations
HRSA	Health Resources and Services Administration
HSCT	post-hematopoietic stem-cell transplantation
HTA	health technology assessment
IFN α	interferon alpha
IH	idiopathic hypersomnia
IM	intramuscular
IND	investigational new drug application
Initial Revolving Credit Facility	our five-year \$500.0 million revolving credit facility under the Credit Agreement entered into in May 2021
Internal Revenue Code	Section 4985 of the Internal Revenue Code of 1986, as amended
InvaGen	InvaGen Pharmaceuticals, Inc., Cipla Ltd., Cipla USA, Inc., and API Pharma Tech LLC
IPR	inter partes review
IPR&D	in-process research and development
IRA	Inflation Reduction Act of 2022
IRS	U.S. Internal Revenue Service
Jazz Investments	Jazz Investments I Limited
Jazz Lux	Jazz Financing Lux S.à.r.l.
Jazz Securities	Jazz Securities Designated Activity Company

Term	Description
KRAS	Kirsten rat sarcoma virus
LBL	lymphoblastic lymphoma
LGS	Lennox-Gastaut syndrome
Ligand	Ligand Pharmaceuticals Incorporated
Lupin	Lupin Inc.
MAA	Marketing Authorization Application
MAPK	mitogen-activated protein kinase
McKesson	McKesson Corporation
MDS	Myelodysplastic Syndrome
MSN	MSN Laboratories Private, Ltd. and MSN Pharmaceuticals, Inc.
NDA	New Drug Application
New Repurchase Program	our share repurchase program announced on July 31, 2024
NHS	U.K. National Health Service
NOL	net operating loss
Non-FAMP	non-federal average manufacturer price
ODE	Orphan Drug Exclusivity in the U.S.
OECD	Organization for Economic Co-operation and Development
OIG	Office of Inspector General of the U.S. Department of Health and Human Services
Old Repurchase Program	our share repurchase program authorized by our board of directors in November 2016
OME	orphan market exclusivity in the EU
Orange Book	FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations"
Otsuka	Otsuka Pharmaceutical Co., Ltd
Padagis	Padagis US LLC
Par	Par Pharmaceutical, Inc.
Patheon	Patheon Pharmaceuticals Inc., together with its affiliates
Patheon Agreement	our Master Manufacturing Services Agreement with Patheon
PBL	Porton Biopharma Limited
PBMs	pharmacy benefit managers
PDUFA	Prescription Drug User Fee Act
Pfenex	Pfenex, Inc.
PharmaMar	Pharma Mar, S.A.
Pillar Two	the OECD framework proposal to implement a two-pillar plan on global tax reform, including a global minimum tax rate of 15% for large multinational corporations on a jurisdiction-by-jurisdiction basis
PRC	People's Republic of China
Protected cell	the cell of a protected cell company, which Jazz invested in in the year ended December 31, 2021
PRSUs	Performance-based restricted stock units
PRV	priority review voucher
PTAB	Patent Trial and Appeal Board of the USPTO
R&D	research and development
R/R	relapsed/refractory
Redx	Redx Pharma plc
REMS	risk evaluation and mitigation strategy
Repricing Amendment No.1	amendment to the Credit Agreement entered into by Jazz Lux in January 2024
Repricing Amendment No.2	amendment to the Credit Agreement entered into by Jazz Lux in July 2024
RFC	Request for Comment
RK Pharma	RK Pharma, Inc., Apicore US LLC, Archis Pharma LLC, Vgyaan Pharmaceuticals LLC

Term	Description
RLD	reference listed drug
Roche	F. Hoffmann-La Roche Ltd
RSUs	restricted stock units
RTOR	Real-Time Oncology Review
sBLA	supplemental Biologics License Application
SCLC	small cell lung cancer
SEC	U.S. Securities and Exchange Commission
Secured Notes	our issued \$1.5 billion in aggregate principal amount of 4.375% senior secured notes, due 2029
Self-Insured Schools Lawsuit	On August 14, 2020, a class action lawsuit was filed in the United States District Court for the Southern District of New York by the Self-Insured Schools of California on behalf of itself and all others similarly situated, against the Company Defendants, as well as Hikma Pharmaceuticals plc, Eurohealth (USA) Inc., Hikma Pharmaceuticals USA, Inc., West-Ward Pharmaceuticals Corp., Roxane Laboratories, Inc., Amneal Pharmaceuticals LLC, Endo International, plc, Endo Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals Inc., Lupin Inc., Sun Pharmaceutical Industries Ltd., Sun Pharmaceutical Holdings USA, Inc., Sun Pharmaceutical Industries, Inc., Ranbaxy Laboratories Ltd., Teva Pharmaceutical Industries Ltd., Watson Laboratories, Inc., Wockhardt Ltd., Morton Grove Pharmaceuticals, Inc., Wockhardt USA LLC, Mallinckrodt plc, and Mallinckrodt LLC
Siegfried	Siegfried USA, LLC and its European affiliates
Simtra	Simtra Biopharma Solutions
SmPC	Summary of Product Characteristics
sNDA	supplemental New Drug Application
Sumitomo	Sumitomo Pharma Co., Ltd
Sunshine provisions	Physician Payment Sunshine Act
sVOD	severe VOD
T-DXd	trastuzumab deruxtecan
Taro	Taro Pharmaceutical Industries Ltd.
TCA	EU-U.K. Trade and Cooperation Agreement
Term SOFR	U.S. dollar Secured Overnight Financing Rate
Teva	Teva Pharmaceuticals, Inc.
Tranche B-1 Dollar Term Loans	upon entry into the Repricing Amendment No.1, the then outstanding Dollar Term Loan was refinanced into a new tranche of U.S. dollar term loans
Tranche B-2 Dollar Term Loans	upon entry into the Repricing Amendment No.2, the then outstanding Tranche B-1 Dollar Term Loans were refinanced into a new tranche of U.S. dollar term loans
Tricare program	Tricare Retail Pharmacy program
TSC	tuberous sclerosis complex
TSR	total shareholder return
U.K. Bribery Act	U.K. Bribery Act of 2010
U.S. GAAP	U.S. generally accepted accounting principles
UFCW Defendants	Jazz Pharmaceuticals Ireland Ltd., Jazz Pharmaceuticals, Inc., Roxane Laboratories, Inc., Hikma Pharmaceuticals plc, Eurohealth (USA), Inc. and West-Ward Pharmaceuticals Corp.
UFCW Lawsuit	On June 30, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by UFCW Local 1500 Welfare Fund on behalf of itself and all others similarly situated, against the UFCW Defendants
UHS Lawsuit	On March 18, 2021, United Healthcare Services, Inc. filed a lawsuit in the United States District Court for the District of Minnesota against the Company Defendants, Hikma Pharmaceuticals plc, Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA) Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., and Lupin Pharmaceuticals, Inc.
USPTO	U.S. Patent and Trademark Office
VA	U.S. Department of Veterans Affairs
VOD	veno-occlusive disease
WAC	Wholesale Acquisition Cost
Werewolf	Werewolf Therapeutics, Inc.
WuXi	WuXi Biologics Co., Ltd.

Term	Description
XLp	XL-protein GmbH
Zepzelca ANDA Filers	Sandoz Inc., InvaGen Pharmaceuticals, Inc., CIPLA USA, Inc. CIPLA (EU) Limited, CIPLA Limited, Zydus Lifesciences Global FZE, Zydus Pharmaceuticals (USA) Inc., Zydus Lifesciences Limited, RK Pharma, Inc., Apicore US LLC, Archis Pharma LLC, Vgyaan Pharmaceuticals LLC, MSN Pharmaceuticals Inc., and MSN Laboratories PVT. LTD.
Zymeworks	Zymeworks Inc.

Products

The brand names of our products, our delivery devices and certain of our product candidates and their associated generic names are given below.

Term	Description
CombiPlex	CombiPlex® (delivery technology platform)
Defitelio	Defitelio® (defibrotide sodium), Defitelio® (defibrotide)
Epidiolex	Epidiolex® (cannabidiol) oral solution, Epidyolex® (the trade name in Europe and other countries outside the U.S. for Epidiolex)
Rylaze	Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn), Enrylaze® (the trade name in Europe and other countries outside the U.S. and Canada for Rylaze)
Sativex	Sativex® (nabiximols) oral solution
Suvecaltamide	Suvecaltamide (JZP385)
Vyxeos	Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion
Xyrem	Xyrem® (sodium oxybate) oral solution
Xywav	Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution
Zepzelca	Zepzelca® (lurbinectedin)
Ziihera	Ziihera® (zanidatamab-hrii)

We own or have rights to various copyrights, trademarks, and trade names used in our business in the U.S. and/or other countries, including the following: Jazz Pharmaceuticals®, Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution, Xyrem® (sodium oxybate) oral solution, Epidiolex® (cannabidiol) oral solution, Epidyolex® (the trade name in Europe and other countries outside the U.S. for Epidiolex), Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn), Enrylaze® (the trade name in Europe and other countries outside the U.S. and Canada for Rylaze), Zepzelca® (lurbinectedin), Defitelio® (defibrotide sodium), Defitelio® (defibrotide), Vyxeos® (daunorubicin and cytarabine) liposome for injection, Vyxeos® liposomal 44 mg/100 mg powder for concentrate for solution for infusion, CombiPlex®, Sativex® (nabiximols) oral solution and Ziihera® (zanidatamab-hrii).

This Annual Report on Form 10-K also includes trademarks, service marks and trade names of other companies. Trademarks, service marks and trade names appearing in this Annual Report on Form 10-K are the property of their respective owners.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the “safe harbor” created by those sections. Forward-looking statements are based on our management’s beliefs and assumptions and on information currently available to our management. In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “could,” “would,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “predict,” “propose,” “intend,” “continue,” “potential,” “possible,” “strive,” “seek,” “designed,” “goal,” “foreseeable,” “likely,” “unforeseen” and similar expressions intended to identify forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance, time frames or achievements to be materially different from any future results, performance, time frames or achievements expressed or implied by the forward-looking statements. We discuss many of these risks, uncertainties and other factors in greater detail under Risk Factors in Part I, Item 1A of this Annual Report on Form 10-K. Given these risks, uncertainties and other factors, you should not place undue reliance on these forward-looking statements. In addition, our goals and objectives are aspirational and are not guarantees or promises that such goals and objectives will be met. Also, these forward-looking statements represent our estimates and assumptions only as of the date of this filing. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. We hereby qualify our forward-looking statements by our cautionary statements. Except as required by law, we assume no obligation to update our forward-looking statements publicly, or to update the reasons that actual results could differ materially from those anticipated in these forward-looking statements, even if new information becomes available in the future.

SUMMARY RISK FACTORS

Below is a summary of material factors that make an investment in our ordinary shares speculative or risky. Importantly, this summary does not address all of the risks and uncertainties that we face. Additional discussion of the risks and uncertainties summarized in this risk factor summary, as well as other risks and uncertainties that we face, can be found under “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K. The below risk factor summary is qualified in its entirety by that more complete discussion of such risks and uncertainties. You should consider carefully the risks and uncertainties described under “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K as part of your evaluation of an investment in our ordinary shares.

- Our inability to maintain revenues from our oxybate franchise would have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products.
- The distribution and sale of our oxybate products are subject to significant regulatory restrictions, including the requirements of a REMS and safety reporting requirements, and these regulatory and safety requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xywav and Xyrem.
- Our inability to maintain or increase sales of Epidiolex/Epidyolex would have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- While we expect Xywav and Epidiolex/Epidyolex to remain our largest products, our success also depends on our ability to effectively commercialize our other existing products and potential future products.
- We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios, and competition from generic drugs.
- Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and other organizations; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement, either of which could diminish our sales or adversely affect our ability to sell our products profitably.
- The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy, including changes to Medicare, may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition.
- In addition to access, coverage and reimbursement, the commercial success of our products depends upon their market acceptance by physicians, patients, third party payors and the medical community.

- Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects.
- Our future success depends on our ability to successfully obtain and maintain regulatory approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.
- We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these transactions.
- Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.
- It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.
- We have incurred, and may in the future incur, substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products.
- Significant disruptions of information technology systems or data security breaches could adversely affect our business.
- We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products.
- If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.
- We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.
- To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate and grow our business.
- If we fail to attract, retain and motivate members of our executive management team and key personnel, our operations and our future growth may be adversely affected.

NOTE REGARDING COMPANY REFERENCE

In this report, unless otherwise indicated or the context otherwise requires, all references to “Jazz Pharmaceuticals,” “Jazz,” “the registrant,” “we,” “us,” and “our” refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries.

Item 1. Business**Overview**

Jazz Pharmaceuticals plc is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases - often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience.

Our strategy for growth is rooted in executing commercial launches and ongoing commercialization initiatives, advancing robust R&D programs and delivering impactful clinical results, effectively deploying capital to strengthen the prospects of achieving our short- and long-term goals through strategic corporate development, and delivering strong financial performance. We focus on patient populations with high unmet needs. We seek to identify and develop differentiated therapies for these patients that we expect will be long-lived assets and that we can support with an efficient commercialization model. In addition, we leverage our efficient, scalable operating model and integrated capabilities across our global infrastructure to effectively reach patients around the world.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

Neuroscience

- **Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution**, a product approved by FDA in July 2020, and launched in the U.S. in November 2020 for the treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy, and also approved by FDA in August 2021 for the treatment of IH in adults and launched in the U.S. in November 2021. Xywav contains 92% less sodium than Xyrem®. Xywav is also approved in Canada for the treatment of cataplexy in patients with narcolepsy.
- **Epidiolex® (cannabidiol) oral solution**, a product approved by FDA and launched in the U.S. in 2018 by GW and currently indicated for the treatment of seizures associated with LGS, DS, or TSC in patients one year of age or older; in the EU and Great Britain (where it is marketed as Epidyolex®) and other markets, it is approved for adjunctive treatment of seizures associated with LGS or DS, in conjunction with clobazam (EU and Great Britain only), in patients 2 years of age and older and for adjunctive treatment of seizures associated with TSC in patients 2 years of age and older.

Oncology

- **Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)**, a product approved by FDA in June 2021 and launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL or LBL in adults and pediatric patients aged one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase. In September 2023, the European Commission granted marketing authorization under the trade name Enrylaze. This therapy is also approved in markets including Great Britain, Canada and Switzerland.
- **Zepzelca® (lurbinectedin)**, a product approved by FDA in June 2020 under FDA's accelerated approval pathway and launched in the U.S. in July 2020 for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy; in Canada, Zepzelca received conditional approval in September 2021 for the treatment of adults with Stage III or metastatic SCLC, who have progressed on or after platinum-containing therapy.
- **Ziihera® (zanidatamab-hrii)**, a product approved by FDA in November 2024 under FDA's accelerated approval pathway and launched in the U.S. in December 2024 for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.

In 2024, consistent with our strategy, we continued to focus on research and development activities within our neuroscience and oncology therapeutic areas. For a summary of our ongoing research and development activities, see "Business—Research and Development" in this Part I, Item 1.

Our Commercialized Products***Neuroscience***

Our Sleep Products. We are the leader in the development and commercialization of oxybate therapy for patients with sleep disorders. Xyrem was approved by FDA in 2002, and is indicated for treating cataplexy and EDS in patients seven years of age or older with narcolepsy. In 2020, we received FDA approval for Xywav for the treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy. In August 2021, Xywav became the first and only therapy approved by FDA for the treatment of IH in adults. Xywav is an oxybate therapy that contains 92% less sodium than Xyrem. Xywav has become a standard of care for patients with narcolepsy and IH.

Xywav. In July 2020, FDA approved Xywav for the treatment of cataplexy and EDS in patients seven years of age and older with narcolepsy. Narcolepsy is a chronic, debilitating neurological disorder characterized by EDS and the inability to regulate sleep-wake cycles normally. Since there is no cure for narcolepsy and long-term disease management is needed, we believe that Xywav represents an important therapeutic option for patients with this sleep disorder. Narcolepsy affects an estimated one in 2,000 people in the U.S., with symptoms typically appearing in childhood. There are five primary symptoms of narcolepsy, including EDS, cataplexy, disrupted nighttime sleep, sleep-related hallucinations, and sleep paralysis. While patients with narcolepsy may not experience all five symptoms, EDS, an essential symptom of narcolepsy, is present in all narcolepsy patients and is characterized by chronic, pervasive sleepiness as well as sudden irresistible and overwhelming urges to sleep (inadvertent naps and sleep attacks). Narcolepsy may affect many areas of life, including limiting a patient's education and employment opportunities, and may lead to difficulties at work, school, or in daily life activities like driving, operating machinery or caring for children. Patients with narcolepsy may also suffer from significant medical comorbidities in both adult and pediatric populations, including increased psychiatric comorbidity (including anxiety disorders and mood disorders), intentional self-injury, attempted suicide, suicide-related mortality, other sleep disorders (such as periodic limb movement disorder), cardiovascular disorders (such as hypertension, coronary atherosclerosis, acute myocardial infarction, and congestive heart failure), and metabolic disorders (such as obesity, metabolic syndrome and diabetes).

Cataplexy, the sudden loss of muscle tone with retained consciousness, can be one of the most debilitating symptoms of narcolepsy. Cataplexy is present in approximately 70% of patients with narcolepsy. Cataplexy can range from slight weakness or a drooping of facial muscles to the complete loss of muscle tone resulting in postural collapse. It may also impair a patient's vision or speech. Cataplexy is often triggered by strong emotions such as laughter, anger or surprise. Cataplexy can severely impair a patient's quality of life and ability to function.

Narcolepsy patients, by virtue of their diagnosis, are at increased risk of cardiovascular events and disease, and the impact of sodium on cardiovascular health is well established. There is also extensive scientific evidence that reducing sodium consumption, which is a modifiable risk factor, is associated with clinically meaningful reductions in blood pressure and cardiovascular disease risk. Therefore, we believe that reducing sodium intake compared to currently-marketed high-sodium oxybate products by 92% each day is a significant advancement for these patients. The 92% reduction of sodium translates into a reduction of approximately 1,000 to 1,500 milligrams per day for a patient prescribed high-sodium oxybate, depending on the dose. Our commercial efforts are focused on educating patients and physicians about the lifelong impact of high sodium intake, and how the use of Xywav enables them to address what is a modifiable risk factor. When patients transition from Xyrem to Xywav, Xywav treatment is initiated at the same dose and regimen (gram for gram) and titrated as needed based on efficacy and tolerability.

We view the adoption of Xywav in narcolepsy as a positive indication that physicians and patients appreciate the benefits of a low-sodium oxybate option. In June 2021, FDA recognized seven years of ODE for Xywav in narcolepsy through July 21, 2027 (which was subsequently extended to January 21, 2028). Nevertheless, Lumryz, a fixed-dose, high-sodium oxybate, was approved by FDA on May 1, 2023 for the treatment of cataplexy or EDS in adults with narcolepsy and was launched in the U.S. market in June 2023. FDA continues to recognize seven years of ODE for Xywav in narcolepsy. In connection with granting ODE for Xywav, FDA stated that "Xywav is clinically superior to Xyrem by means of greater safety because Xywav provides a greatly reduced chronic sodium burden compared to Xyrem." FDA's summary also stated that "the differences in the sodium content of the two products at the recommended doses will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated." FDA has also recognized that the difference in sodium content between Xywav and Lumryz is likely to be clinically meaningful in all patients with narcolepsy and that Xywav is safer than Lumryz in all such patients. Lumryz has the same sodium content as Xyrem. Xywav is the only approved oxybate therapy that does not carry a warning and precaution related to high sodium intake.

On August 12, 2021, FDA approved Xywav for the treatment of IH in adults. Xywav remains the first and only FDA-approved therapy to treat IH. We initiated the U.S. commercial launch of Xywav for the treatment of IH in adults on November 1, 2021. In January 2022, FDA recognized seven years of ODE for Xywav in IH through August 12, 2028. IH is a debilitating neurologic sleep disorder characterized by chronic EDS (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness), severe sleep inertia, and prolonged and

non-restorative nighttime sleep. Although there are overlapping clinical features with other conditions, including narcolepsy, IH has its own specific diagnostic criteria. IH can significantly affect social, educational and occupational functioning. An estimated 37,000 people in the U.S. have been diagnosed with IH and are actively seeking healthcare.

We have agreements in place for Xywav with all three major PBMs in the U.S. To date, we have entered into agreements with various entities and have achieved benefit coverage for Xywav in both narcolepsy and IH indications for approximately 90% of commercial lives.

We have seen strong adoption of Xywav in narcolepsy since its launch in November 2020 and increasing adoption in IH since its launch in November 2021. In 2024, net product sales of Xywav were \$1,473.2 million, which represented 39% of our total net product sales for the year.

Xyrem. Xyrem was approved in the U.S. for the treatment of cataplexy in patients with narcolepsy in 2002 and was approved for treatment of EDS in patients with narcolepsy in 2005. In October 2018, Xyrem was also approved in the U.S. for the treatment of cataplexy or EDS in pediatric patients seven years of age and older with narcolepsy.

In 2024, net product sales of Xyrem were \$233.8 million, which represented 6% of our total net product sales for the year.

Xywav and Xyrem REMS. Our marketing, sales and distribution of Xywav and Xyrem in the U.S. are subject to a REMS, which is required by FDA to mitigate the risks of serious adverse outcomes resulting from inappropriate prescribing, abuse, misuse and diversion of Xywav and Xyrem. The Xywav and Xyrem REMS has the same requirements for both products. Under this REMS, all of the Xywav and Xyrem sold in the U.S. must be dispensed and shipped directly to patients or caregivers through a central pharmacy. Xywav and Xyrem may not be stocked in retail pharmacies. Physicians and patients must complete an enrollment process prior to fulfillment of Xywav and Xyrem prescriptions, and each physician and patient must receive materials concerning the serious risks associated with Xywav and Xyrem before the physician can prescribe, or a patient can receive, the product. The central certified pharmacy must monitor and report instances of patient or prescriber behavior giving rise to a reasonable suspicion of abuse, misuse or diversion of Xywav and Xyrem, and maintains enrollment and prescription monitoring information in a central database. The central pharmacy ships the product directly to the patient (or caregiver) by a courier service.

Since 2002, we have had exclusive agreements with ESSDS, the central pharmacy for Xywav and Xyrem, to distribute Xywav and Xyrem in the U.S. and provide patient support services related to Xyrem. In December 2022, we entered into new agreements with ESSDS with a two-year term and our ability to extend the term for an additional year. Our current agreements with ESSDS, which expire on December 31, 2025, may be terminated by either party at any time without cause on 180 days' prior written notice to the other party.

Epidiolex. We acquired Epidiolex (Epidyolex outside the U.S.) in May 2021 as part of our GW Acquisition, which expanded our growing neuroscience business with a global, high-growth childhood-onset epilepsy franchise. Epidiolex was approved in the U.S. in June 2018 for the treatment of seizures associated with two rare and severe forms of epilepsy, LGS and DS, in patients two years of age and older, and subsequently approved in July 2020 for the treatment of seizures associated with TSC in patients one year of age and older. FDA also approved the expansion of the other approved indications, LGS and DS, to patients one year of age and older. In September 2019, the EC granted marketing authorization under the trade name Epidyolex for use as adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients two years of age and older. Epidyolex is now launched in all five key European markets: United Kingdom, Germany, Italy, Spain and France. The clobazam restriction is limited to the EU and Great Britain. Epidyolex was also approved for adjunctive therapy in seizures associated with TSC for patients 2 years of age and older in the EU in April 2021 and Great Britain in August 2021, and is approved for this indication in other markets. Epidiolex/Epidyolex is also approved in markets including Switzerland, Israel, Canada, and Australia. See "Research and Development" below for a discussion of clinical development activities for Epidiolex.

LGS and DS are severe childhood-onset, drug-resistant epilepsy syndromes. LGS and DS affect approximately 35,000-50,000 and approximately 10,000 individuals in the U.S., respectively. TSC is a rare genetic disorder that causes non-malignant tumors to form in many different organs and is a leading cause of genetic epilepsy. TSC affects approximately 50,000 individuals in the U.S. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027.

Net product sales of Epidiolex/Epidyolex in 2024 were \$972.4 million, which represented 25% of our total net product sales for the year.

Oncology

Rylaze. Rylaze was approved by FDA in June 2021 under the RTOR program, and was launched in the U.S. in July 2021, for use as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL, and LBL, in pediatric

and adult patients one month and older who have developed hypersensitivity to E. coli-derived asparaginase. Rylaze is the only recombinant Erwinia asparaginase manufactured product that maintains a clinically meaningful level of serum asparaginase activity throughout the entire intended course of treatment. We developed Rylaze to address the needs of patients and health care providers for an innovative, high-quality Erwinia asparaginase with reliable supply. See “Research and Development” below for a discussion of clinical development activities for Rylaze.

The initial approved recommended dosage of Rylaze was for an IM administration of 25 mg/m² every 48 hours. In November 2022, FDA approved an sBLA, for a Monday/Wednesday/Friday 25/25/50 mg/m² IM dosing schedule. In September 2023, the EC granted marketing authorization for JZP458 (Rylaze) under the trade name Enrylaze. Enrylaze was approved in Great Britain in January 2024, and is approved in other markets.

In 2024, net product sales of Rylaze were \$410.8 million, which represented 11% of our total net product sales for the year.

Zepzelca. We acquired U.S. development and commercialization rights to Zepzelca in early 2020, and launched six months thereafter, with an indication for treatment of patients with SCLC with disease progression on or after platinum-based chemotherapy. Zepzelca is an alkylating drug that binds guanine residues within DNA. This triggers a cascade of events that can affect the activity of DNA binding proteins, including some transcription factors, and DNA repair pathways, resulting in disruption of the cell cycle and eventual cell death. Our education and promotional efforts are focused on SCLC-treating physicians. We are continuing to raise awareness of Zepzelca across academic and community cancer centers.

Our exclusive U.S. development and commercialization rights to Zepzelca were acquired through an exclusive license agreement we entered into with PharmaMar in December 2019. In October 2020, we entered into an amendment to the license agreement with PharmaMar to expand our exclusive license to include rights to develop and commercialize Zepzelca in Canada. The term of the amended license agreement extends on a licensed product-by-licensed product and country-by-country basis until the latest of: (i) expiration of the last PharmaMar patent covering Zepzelca in that country (subject to certain exclusions), (ii) expiration of regulatory exclusivity for Zepzelca in that country and (iii) 12 years after the first commercial sale of Zepzelca in that country. We have the right to terminate the amended license agreement at will upon a specified notice period, and either party can terminate the amended license agreement for the other party’s uncured material breach or bankruptcy.

Zepzelca was granted orphan drug designation for adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy by FDA in August 2018. In December 2019, PharmaMar submitted an NDA, to FDA for accelerated approval of Zepzelca for relapsed SCLC based on data from a Phase 2 trial, and in February 2020, FDA accepted the NDA for filing with priority review. In June 2020, FDA granted accelerated approval of Zepzelca for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy. Zepzelca is approved based on response rate and duration of response. In collaboration with Roche, we have an ongoing Phase 3 pivotal clinical trial for Zepzelca for use as maintenance therapy in first-line extensive-stage SCLC in combination with Tecentriq® (atezolizumab) following induction therapy with carboplatin, etoposide and Tecentriq. In October 2024, we announced positive top-line results from the trial showing a statistically significant and clinically meaningful benefit for Zepzelca and atezolizumab in combination in the first-line maintenance setting. We plan to submit a sNDA in the first half of 2025 to support approval of this combination in the first-line maintenance setting. In addition, our licensor PharmaMar is conducting a confirmatory trial in second-line SCLC. This is a three-arm trial comparing Zepzelca as either monotherapy or in combination with irinotecan to investigator’s choice of irinotecan or topotecan. Data from either the first-line maintenance trial of Zepzelca in combination with Tecentriq or the PharmaMar trial could serve to confirm clinical benefit of Zepzelca and support full approval in the U.S. See “Research and Development” below for a discussion of clinical development activities for Zepzelca.

In 2024, net product sales of Zepzelca were \$320.3 million, which represented 8% of our total net product sales for the year.

Ziihera. We acquired our exclusive development and commercialization rights to Ziihera in 2022 through a licensing agreement with a subsidiary of Zymeworks providing development and commercialization rights to zanidatamab across all indications in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. The term of the license agreement extends on a licensed product-by-licensed product and country-by-country basis until the expiration of the royalty term for such licensed product in such country. We have the right to terminate the license agreement at will upon a specified notice period, and either party can terminate the license agreement for the other party’s uncured material breach or bankruptcy.

Ziihera is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrII with HER2 results in internalization leading to a reduction of the receptor on the tumor cell surface. In the U.S., Ziihera is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test. Ziihera was launched in December 2024.

In 2024, net product sales of Ziihera were \$1.1 million, which represented less than 1% of our total net product sales for the year.

Revenue Diversification

As part of our objective to build a durable, growing commercial portfolio and reduce business risk by diversifying our revenue sources, we have been actively seeking to expand our commercial portfolio through a combination of launching internally developed therapies and commercial assets or investigational therapies acquired through corporate development. In 2020, 74% of total revenue was generated by one product, the high-sodium oxybate Xyrem. For the year ended December 31, 2024, 11% of total revenue was generated by Xyrem plus high-sodium oxybate AG royalty revenue.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

<u>Product</u>	<u>Indications</u>	<u>Initial Approval Date</u>	<u>Markets</u>
NEUROSCIENCE			
Xywav® (calcium, magnesium, potassium, and sodium oxybates)	Treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy.	July 2020	U.S.
	Treatment of IH in adults.	August 2021	U.S.
	Treatment of cataplexy in patients with narcolepsy.	May 2023	Canada
Epidiolex® (cannabidiol)	Treatment of seizures associated with LGS, DS, or TSC, in patients 1 year of age and older.	June 2018	U.S.
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older. ¹	September 2019	EU, Great Britain, EEA, Israel, Switzerland, Australia, other markets
	For adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.	April 2021	EU, Great Britain, Israel and Switzerland
Epidiolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS, DS or TSC for patients 2 years of age and older.	November 2023	Canada
ONCOLOGY			
Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL or LBL in adult and pediatric patients 1 month or older who have developed hypersensitivity to E. coli-derived asparaginase.	June 2021	U.S.
Rylaze® (crisantaspase recombinant)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL, in adults and pediatric patients 1 year or older who have developed hypersensitivity to E. coli-derived asparaginase.	September 2022	Canada
Enrylaze® (recombinant crisantaspase)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL in adult and pediatric patients (1 month and older) who have developed hypersensitivity or silent inactivation to E. coli-derived asparaginase.	September 2023	EU, Great Britain, Switzerland, other markets
Zepzelca® (lurbinectedin)	Treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy.	June 2020	U.S. (licensed from PharmaMar) ²
	Treatment of adults with Stage III or metastatic SCLC who have progressed on or after platinum-containing therapy.	September 2021	Canada (licensed from PharmaMar) ³
Ziihera® (zanidatamab-hrii)	Treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.	November 2024	U.S. (licensed from Zymeworks) ²

¹ The clobazam restriction limited to EU and Great Britain

² Accelerated approval received from FDA

³ Conditional approval received from Health Canada

Research and Development Progress

Our research and development activities encompass all stages of development and currently include clinical testing of new product candidates and activities related to clinical improvements of, or additional indications or new clinical data for, our existing marketed products. We also have active preclinical programs for novel therapies, including neuroscience and precision medicines in oncology. We are increasingly leveraging our growing internal research and development function, and we have also entered into collaborations with third parties for the research and development of innovative early-stage product candidates and have supported additional investigator-sponsored trials that are anticipated to generate additional data related to our products. We also seek out investment opportunities in support of the development of early- and mid-stage technologies in our therapeutic areas and adjacencies. We have a number of licensing and collaboration agreements with third parties, including biotechnology companies, academic institutions and research-based companies and institutions, related to preclinical and clinical research and development activities in hematology and in precision oncology, as well as in neuroscience.

Oncology

Zanidatamab. Zanidatamab is a HER2-targeted bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Zanidatamab is currently being evaluated in multiple clinical trials as a treatment for patients with HER2-expressing cancers. In November 2024, we announced that zanidatamab had been approved by FDA for treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test. We have an ongoing Phase 3 randomized clinical trial evaluating zanidatamab in combination with chemotherapy plus or minus tislelizumab as a first-line treatment for HER2-expressing GEA, an ongoing Phase 2 trial examining zanidatamab in combination with chemotherapy in first-line patients with HER2-expressing metastatic GEA and an ongoing Phase 3 trial examining zanidatamab in first-line patients with HER2-positive BTC. There are also multiple ongoing clinical trials exploring zanidatamab in breast cancer and other HER2-expressing tumor types.

Zepzelca. Our development plan for Zepzelca continues to progress.

In collaboration with Roche, we have an ongoing Phase 3 pivotal clinical trial in use as maintenance therapy in first-line extensive-stage SCLC of Zepzelca in combination with Tecentriq® (atezolizumab). In October 2024, we announced positive top-line results from the trial showing a statistically significant and clinically meaningful benefit for Zepzelca and atezolizumab in combination in the first-line maintenance setting. In addition, our licensor PharmaMar is conducting a confirmatory trial in second-line SCLC. This is a three-arm trial comparing Zepzelca as either monotherapy or in combination with irinotecan to investigator's choice of irinotecan or topotecan. Data from either the first-line maintenance trial of Zepzelca in combination with Tecentriq or the PharmaMar trial could serve to confirm clinical benefit of Zepzelca and support full approval in the U.S.

We have an ongoing Phase 4 observational study to collect real world safety and outcome data in adult Zepzelca monotherapy patients with SCLC who progress on or after prior platinum-containing chemotherapy.

JZP815. JZP815 is a pan-RAF kinase inhibitor that targets specific components of the MAPK pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer. In October 2022, we enrolled our first patient in a Phase 1 study to investigate the safety, dosing, and initial antitumor activity of JZP815 in participants with advanced or metastatic solid tumors harboring alterations in the MAPK pathway.

JZP898. JZP898 is a differentiated, conditionally-activated IFN α INDUKINE™ molecule. We acquired rights to JZP898 from Werewolf in 2022 under an exclusive, worldwide, royalty-bearing license to develop, manufacture and commercialize Werewolf's investigational WTX-613, now referred to as JZP898. In November 2023, we enrolled our first patient in a Phase 1 study to investigate the safety, tolerability, pharmacokinetics, immunogenicity and preliminary antitumor activity of JZP898 both as a monotherapy and in combination with pembrolizumab in adults with advanced/metastatic solid tumors.

Neuroscience

Epidiolex. We have an ongoing Phase 3 trial of Epidiolex for LGS, DS and TSC in Japan. In August 2024, we announced top-line results from the trial. The trial did not meet the primary efficacy endpoint of a pre-specified percentage change in indication-associated seizure frequency during the treatment period (up to 16 weeks) compared to baseline in Japanese pediatric patients; however, numeric improvements were observed in the primary and several secondary endpoints. No new safety signals were observed in the trial. We are continuing to collect data in Japanese patients and plan to engage with regulatory authorities in Japan regarding a potential new drug application.

JZP441. JZP441 is a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. In May 2022, we announced that we had entered into a licensing agreement with Sumitomo to acquire exclusive development and commercialization rights in the U.S., Europe and other territories for DSP-0187, now referred to as JZP441. Sumitomo initiated a Phase 1 trial in Japan in November 2021 to evaluate safety, tolerability and pharmacokinetics of JZP441 in healthy volunteers. In November 2022, we initiated a Phase 1 development

program to assess the safety, tolerability, pharmacokinetics, and pharmacodynamics of JZP441 in sleep-deprived healthy volunteers. In November 2023, we announced that the study achieved proof of concept in healthy volunteers based on the Maintenance of Wakefulness Test and that the program was being paused as we analyzed safety findings related to visual disturbances and cardiovascular effects; no liver toxicity signals were observed. Following additional review of the trial findings and input from FDA, we plan to initiate a small Phase 1b trial of JZP441 in narcolepsy Type 1 patients in 2025. We expect data from this trial will further our understanding of JZP441 and orexin-2 receptor agonism, providing learnings that could inform potential future development efforts.

We are also pursuing early-stage activities related to the development of JZP324, an extended-release low sodium oxybate formulation that we believe could provide a clinically meaningful option for patients with serious sleep disorders.

Preclinical

Through third parties, we are also pursuing oncology and neuroscience preclinical and clinical research and development activities under a number of licensing and collaboration agreements, including with:

- XLP for rights to use XLP's PASylation® technology to extend the plasma half-life of selected asparaginase product candidates;
- Redx for preclinical collaboration activities related to the Ras/Raf/MAP kinase pathway program that we purchased from Redx;
- We are also evaluating the use of our CombiPlex delivery technology platform in a number of therapeutic formulations and combinations in oncology as part of our internal oncology research and development activities; and
- Autifony to collaborate on discovering and developing drug candidates targeting two different ion channel targets associated with neurological disorders.

Below is a summary of our key ongoing and planned development projects related to our products and pipeline and their corresponding current stages of development:

<u>Product Candidates</u>	<u>Description</u>
ONCOLOGY	
Regulatory Review	
Zanidatamab	Second-line HER2-expressing BTC (under EMA review)
Phase 3	
Zanidatamab	First-line HER2-positive GEA (ongoing trial)
Zanidatamab	First-line HER2-positive BTC (ongoing trial)
Zanidatamab	Previously treated HER2-positive breast cancer in patients whose disease has progressed on previous T-DXd treatment (EmpowHER-BC-303) (ongoing trial)
Zepzelca	First-line maintenance for extensive-stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing trial) Confirmatory second-line trial (PharmaMar study) (ongoing trial)
Vyxeos	AML or MDS (AML18) (cooperative group studies) (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing trial) Newly diagnosed pediatric patients with AML (COG cooperative group study) (ongoing trial)
Phase 2	
Zanidatamab	HER2-expressing GEA, BTC or colorectal cancer in combination with standard first-line chemotherapy (ongoing trial)
Zanidatamab	Basket trial including HER2-positive solid tumors (DiscovHER-Pan-206) (ongoing trial)
Vyxeos	High-risk MDS (European Myelodysplastic Syndromes) (cooperative group study) (ongoing trial) Newly diagnosed untreated patients with intermediate- and high-risk AML (cooperative group study) (ongoing trial)
Vyxeos + other approved therapies	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study) (ongoing trial) De novo or R/R AML (MD Anderson collaboration study) (ongoing trial)
Phase 2a	

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Zanidatamab	Previously treated HER2+ HR+ breast cancer in combination with palbociclib (ongoing trial)
Phase 1b/2	
Zanidatamab	First-line breast cancer and GEA (BeiGene trial) (ongoing trial)
Zanidatamab	HER2-expressing breast cancer in combination with ALX148 (ongoing trial)
Phase 1	
JZP815	Raf and Ras mutant tumors (acquired from Redx) (ongoing trial)
Zanidatamab	Previously treated metastatic HER2-expressing cancers in combination with select antineoplastic therapies (cooperative group study) (ongoing trial)
JZP898	Conditionally-activated IFN α INDUKINE™ molecule in solid tumors (ongoing trial)
Vyxeos	Low intensity dosing for higher risk MDS (MD Anderson collaboration study) (ongoing trial)
Preclinical	
KRAS inhibitor targets	G12D selective and pan-KRAS molecules (acquired from Redx)
Undisclosed targets	Oncology
CombiPlex®	Hematology/oncology exploratory activities
NEUROSCIENCE	
Phase 3	
Epidyolex	LGS, TSC and DS (ongoing trial in Japan)
Phase 1	
JZP324	Oxybate extended-release formulation (planned trial)
JZP441*	Potent, highly selective oral orexin-2 receptor agonist (ongoing trial)
Preclinical	
Undisclosed targets	Sleep Epilepsy Other Neuroscience

*Also known as DSP-0187 (see discussion above in this section for JZP441)

Commercialization Activities

We have direct Jazz commercial operations in the U.S., Europe, Australia and Canada and a network of commercial distributors that represent our commercial interests in other key markets across the globe. In the U.S., our products are commercialized through a number of teams, including a team of experienced, trained sales professionals who provide education and promote Xywav, Epidiolex, Zepzelca, Rylaze, Ziihera, Vyxeos and Defitelio to healthcare providers in the appropriate specialties for each product. In addition, we have a team that interacts with payors and institutions to ensure access and coverage for the products, as well as Xyrem, and a team that distributes the products throughout the U.S. healthcare system (wholesalers, pharmacies, hospitals, and community and academic institutions) and provides patient services.

In Canada and in approved markets in Europe and Australia where we commercialize Defitelio and Vyxeos, we have a field force of hematology sales specialists. In markets where these products either are not approved or are unable to be promoted under local regulation, we have medical affairs personnel responsible for responding to medical information requests and for providing information consistent with local treatment protocols with respect to such products. In certain European markets and Australia, we have a sales team and a team of medical science liaisons supporting our commercialization of Epidyolex. In addition, we directly market Xywav, Xyrem and Rylaze in Canada.

Other commercial activities include marketing related services, pricing and access, industry analytics and insights, distribution services and commercial support services. We employ third party vendors, such as advertising agencies, market research firms and suppliers of marketing and other sales support-related services, to assist with our commercial activities. We also provide reimbursement and patient assistance support for our U.S. markets.

We intend to scale the size of our sales force as appropriate to effectively reach our target audience in the specialty markets in which we currently operate. We promote Zepzelca, Rylaze, Vyxeos, Defitelio and Ziihera to many hematology and oncology specialists who operate in the same hospitals and outpatient clinical sites, and we believe that we benefit from

operational synergies from this overlap. Continued growth of our current marketed products and the launch of any future products may require a reevaluation of our field force and support organization in and outside the U.S.

High Performance Organization and Human Capital Management

We are committed to creating a high performing company where the culture embodies our corporate purpose to innovate to transform the lives of patients and reflects our key goals: (1) be a purpose-driven, people-centric, and great place to work and (2) live our core values of Integrity, Collaboration, Passion, Innovation, and Pursuit of Excellence.

Employee Demographics. As of December 31, 2024, Jazz employed approximately 2,800 people worldwide, of which approximately 50% were employed in the U.S. and approximately 50% were employed outside the U.S., primarily in the U.K., Ireland and across the EU. As an innovative biopharmaceutical company, we have over 740 employees — representing approximately 27% of our global workforce — supporting our research and development activities. We consider our employee relations to be good.

Company Culture. We believe a culture rooted in purpose, centered on people, and focused on performance is key to unlocking our full potential and achieving sustainable success. By prioritizing a people-centric and performance-based approach, we aim to create a workplace where purpose fuels passion, leading to innovative solutions and exceptional business outcomes.

We aim to create an environment where our employees live our core values to unlock the full potential of our people as a key to driving business performance. We are committed to fostering an inclusive environment where all employees feel they belong, which in turn brings a variety of perspectives that drive innovation and business success. We strive to create a workplace culture that fosters the ability of our employees to be their authentic selves and contribute boldly. Our belonging and inclusion strategy includes: (1) cultivating a workforce that reflects unique backgrounds, experiences, and talents and represents the varied perspectives of the patients and customers we serve; (2) investing in talent development and ensuring equal opportunities for all; and (3) creating a culture of inclusion and belonging. As of December 31, 2024,

- 50% of our board of directors and 56% of our executive committee is diverse in terms of gender, ethnicity and/or sexual orientation.
- Women represent 55% of our global workforce and 46% at the leadership level (employees at executive director and above).
- In the U.S., people of color represent 35% of our U.S. workforce and 20% at the leadership level.

We believe an employee population that reflects the communities that we serve and a culture that fosters belonging and inclusion leads to innovation, employee engagement, and strong business performance. We have created various employee resource groups with membership open to all employees consisting of three ConcERTos, and six Affinity Forums representing the wide variety of backgrounds of our employees and providing a platform for broader company engagement and education. Our ConcERTos and Affinity Forums were established as broad self-led teams of employee volunteers with varied backgrounds and perspectives with the aim of connecting Jazz employees with similar visions and interests in inclusive, welcoming, and collaborative settings. As of the end of 2024, 37% of our global workforce were active in at least one of these groups.

While we are proud of what we have accomplished to date, we remain committed to our aspiration of providing an inclusive and high-performing workplace that is supportive of all backgrounds, including among our broader leadership.

Employee Engagement. We have a strong employee value proposition anchored in our shared commitment to our purpose to innovate to transform the lives of patients and their families. We believe employee engagement and the power of our employee voices is foundational to employee belonging and strong performance. We have transparent and regular communication channels with our employees consisting of many forms — including all employee meetings, regular communication messages from executive leadership, town halls, top leadership forums, pulse check feedback mechanisms and employee feedback surveys.

Our employee feedback surveys are designed to help us measure overall employee engagement as well as gather insights on other important areas of our employee experience, and we consistently achieve participation rates above 75%. We consistently have high levels of engagement as measured by employees' feelings of connection to our purpose, a sense of belonging, as well as Jazz being considered a good place to work by our employees. We continue to focus on high-performance practices we have deemed critical, such as decision-making, planning and prioritizing work, speaking up and constructive challenge, accountability, and a growth mindset. Our survey informs programs and activities aligned with achieving our corporate objectives and achieving our goal of evolving our operating culture for agility and scalability.

Our Community Beat ConcERTo is made up of employee volunteer teams that promote company culture and create a sense of belonging and camaraderie among our employees. They organize programs and engagement activities on a local level to connect employees with the company strategy and business goals, support local communities, and promote employee health

and well-being initiatives. They play a pivotal role in fostering community within our working model by engaging remote employees and maximizing connection during times together at our sites and offices.

Growth, Development and Total Rewards. Our talent strategy focuses on attracting the best talent, recognizing and rewarding the performance of our employees as defined by both what they accomplished and how they accomplished it, and continually developing our talent through new experiences and learning opportunities. We believe there is ample opportunity for growth and development at Jazz and there is not a one size fits all approach to growing our talent. We strive to create the best career experience for all of our employees and encourage them to have regular dialogue with their leadership to create meaningful career development plans.

Our performance management process supports our culture of continual feedback and coaching, and ongoing growth and development through new experiences and learning. We encourage all employees to have an individual development plan to outline learning and growth interests and focus areas.

We leverage digital learning platforms to provide on demand, bite-sized learning to all employees that can be accessed 24/7 on a range of topics from leadership, personal effectiveness and well-being. In addition, we provide a number of self-service learning resources via our intranet site on topics such as High-Performance Teamwork, Decision Making, Hybrid Working, and Digital Skills development. We continue to offer tuition reimbursement in our major markets aimed at growth and career development.

In 2024, we continued to focus on developing the capabilities of our Global Leadership Team (Top 80 leaders) to build leadership excellence, strengthen relationships, and encourage cross functional collaboration in pursuit of our enterprise strategic goals. Our focus in 2024 was on building people manager excellence and behaviors linked to a high-performance culture, e.g., how to create an environment where people feel able to constructively challenge one another.

Our management and leadership teams place significant focus and attention to capability development and succession planning for critical roles. We regularly review talent development and succession plans for each of our functions to successfully maintain business operations and develop a pipeline of talent.

We provide our employees with what we believe to be market competitive and locally relevant compensation and benefits that support our overarching strategy to attract, retain and reward highly talented employees in an extremely competitive and dynamic industry. This includes broad-based participation in our annual incentive plan, which rewards employees based on the company's achievement of pre-established goals (or sales targets in the case of sales incentive plans) as well as performance against their personal objectives and our long-term equity incentive plans, which fosters an ownership culture and provides eligible employees with the opportunity to share in the long-term success they help create.

Fundamental to creating a high performing company is our commitment to building and maintaining a culture of health and wellbeing throughout the organization. We do this by supporting employees and their families through access to a suite of innovative programs that inspire them to focus on their mind, body, finances and work/life balance.

- We provide a robust set of offerings centered on mental and emotional health, including resilience, stress management, mindfulness and managing clinical conditions.
- We offer programs that promote activity, healthy nutrition habits, chronic condition prevention and early detection of more serious disease/illness.
- We offer an enhanced suite of global paid leave and other time-off policies to address the differing needs of our employee population through varying stages of life, including minimum standards for new parent leave (irrespective of gender or how a family is created), family caregiver leave and bereavement leave. We offer a global volunteer day to provide employees time off with full pay to give back to their communities.
- Our Wellbeing Reimbursement Account reimburses employees for a wide array of expenses that support their overall wellbeing, empowering them to choose what is most important to them.
- In 2025, we will hold our first-ever Jazz Wellbeing Week, providing dedicated time off to all employees to focus on wellbeing and self-care.

Employee Care. We are committed to providing a great workplace experience where people feel invested in, valued and cared for, and a sense of belonging. We strive to enable our employees to live into our values and support one another while doing everything we can to deliver on our patient mission. Important to this are leader expectations and tools given the rise and complexity of emerging employee demands and needs – including more flexibility to address personal needs, a greater connection to understand the whole person and their lives, and creating supportive and productive work environments for people to thrive. We provide productivity and collaboration tools and resources for employees working remotely, including training and toolkits to help leaders effectively lead and manage remote teams; increased flexibility within work schedules and leave programs to support employees caring for children and others; expanded employees assistance and mindfulness programs

to help employees and their families manage anxiety, stress, and overall wellbeing; and increased investment in resources focused on inclusion and belonging.

Through direct input from employees, external insights and best practices, we developed our flexible working model; expanding the power of intentional collaboration and our ability to more effectively manage our global and highly distributed team workforce. This approach to work, called “Jazz Remix,” aims to provide eligible employees with the greatest flexibility and agility to globally connect, collaborate, innovate and perform.

Environment, Health and Safety. Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Ireland, the U.K. and Italy where we have manufacturing facilities. Our manufacturing activities involve the controlled storage, use and disposal of chemicals and solvents. Environmental and health and safety authorities in Ireland, the U.K. and Italy administer laws governing, among other matters, the emission of pollutants into the air (including the workplace), the discharge of pollutants into bodies of water, the storage, use, handling and disposal of hazardous substances, the exposure of persons to hazardous substances, and the general health, safety and welfare of employees and members of the public. In certain cases, such laws, directives and regulations may impose strict liability for pollution of the environment and contamination resulting from spills, disposals or other releases of hazardous substances or waste. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

We seek to operate our manufacturing facilities in an environmentally responsible way to protect our people, our business, our environment and the local communities in which we operate. In light of the potential impact of our business on the environment, we have adopted a number of internal environmental policies and management systems designed to manage our operations in compliance with applicable laws, directives and regulations on environmental protection and in support of environmental sustainability and local biodiversity. Our environmental policies and management systems include procedures for assessing compliance with applicable environmental laws and regulations and reporting incidents of non-compliance to applicable governmental authorities. For example, we have environmental policies governing our manufacturing facilities in Ireland, the U.K. and Italy, which demonstrate our commitment to environmental sustainability and require us to minimize resource use (e.g., energy and water) and waste generation, optimize the use of raw materials, and undertake continuous improvement in environmental performance, with an emphasis on pollution prevention.

Competition

The biopharmaceutical industry is highly competitive. Our products compete, and our product candidates may in the future compete, with currently existing therapies, product candidates currently under development by us and others and/or future product candidates, including new chemical entities that may be safer, more effective or more convenient than our products. Any products that we develop may be commercialized in competitive markets, and our competitors, which include large global pharmaceutical companies and small research-based companies and institutions, may succeed in developing products that render our products obsolete or noncompetitive.

With respect to competition we face from generic drugs, certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. Generic competition often results in decreases in the net prices at which branded products can be sold.

In particular, our products and most advanced product candidates face or may face competition as described below:

- *Xywav and Xyrem.* Xywav and Xyrem are approved by FDA and marketed in the U.S. for the treatment of both cataplexy and EDS in both adult and pediatric patients with narcolepsy. We and others have launched products to treat EDS in narcolepsy and may in the future launch products to treat cataplexy in narcolepsy that are competitive with or disrupt the market. Xywav and Xyrem face competition from Avadel’s Lumryz, a branded product for treatment of cataplexy and/or EDS in narcolepsy. Lumryz, a once-nightly dose, high-sodium oxybate, was launched in the U.S. market in June 2023. We and Avadel are engaged in various litigation regarding Lumryz and our oxybate products. We cannot at this time predict the timing or ultimate outcome of the litigation or the impact of the litigation on our sleep products, Xywav and Xyrem. For additional information on litigation involving this matter, see “*FDA Litigation*” and “*Avadel Litigation*” in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

In addition, since January 2023 our oxybate products have faced competition from AG high-sodium oxybate pursuant to a settlement agreement we entered into with an ANDA filer, and since July 2023, an additional AG version of

high-sodium oxybate from a volume-limited ANDA filer. Collectively, these AG versions of high-sodium oxybate have negatively impacted and are expected to continue to negatively impact Xyrem and Xywav sales for patients with narcolepsy. Specifically, a wholly owned subsidiary of Hikma launched its AG version of high-sodium oxybate in January 2023 and Amneal launched its AG version of high-sodium oxybate in July 2023. Hikma has elected to continue to sell the Hikma AG product, with royalties to be paid to us, for a total of up to four years beginning in January 2024, which election may be terminated by Hikma in accordance with the notice provisions in the agreements between the parties. We have the right to receive a meaningful royalty from Hikma on net sales of the Hikma AG product; the royalty rate was fixed for the second half of 2023. There was also a substantial increase in the royalty rate beginning in January 2024, which will remain fixed for the duration of the agreement's term. For a description of generic versions of sodium oxybate and/or new products for the treatment of cataplexy and/or EDS that currently compete or could in the future compete with, or otherwise disrupt the market for, Xywav and Xyrem, as well as a description of our settlement agreements with ANDA filers, see the risk factor under the heading *"The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products"* in Part I, Item 1A of this Annual Report on Form 10-K.

In addition, Xywav and Xyrem may face competition in the future from other new sodium oxybate formulations for treatment of narcolepsy. Also, in the future we expect competition from generic versions of sodium oxybate. For example, we received notices in June 2021 and February 2023, that Lupin and Teva, respectively, filed ANDAs for generic versions of Xywav. On October 13, 2023, Lupin announced that it has received tentative approval for its application to market a generic version of Xywav.

Non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy or IH (Xywav is the first and only FDA-approved therapy to treat IH), including new market entrants, even if not directly competitive with Xywav or Xyrem, could have the effect of changing treatment regimens and payor or formulary coverage of Xywav or Xyrem in favor of other products, and indirectly materially and adversely affect sales of Xywav and Xyrem. Xywav and Xyrem face competition from Sunosi, which we sold to Axsome in 2022. Xywav and Xyrem may face increased competition from new branded entrants to treat EDS or cataplexy in narcolepsy such as pitolisant, which has been approved by FDA for the treatment of both cataplexy and EDS in adult patients with narcolepsy. Harmony Biosciences has announced a phase 3 study for pitolisant for IH after receiving a refusal to file from FDA in February 2025. Other companies have announced that they have product candidates in various phases of development to treat the symptoms of narcolepsy, such as Axsome's reboxetine, and various companies are performing research on orexin agonists for the treatment of sleep disorders, including Takeda Pharmaceutical Company Limited, Merck & Co., Inc., Eisai Co., Ltd., Centessa Pharmaceuticals plc and Alkermes plc.

In addition, we are also aware that prescribers often prescribe branded or generic medications for cataplexy and IH before prescribing or instead of prescribing oxybate therapy, and that payors often require patients to try such medications before they will cover Xywav or Xyrem, even if they are not approved for this use. For example, prescribers often treat mild cataplexy with drugs that have not been approved by FDA for this indication, including tricyclic antidepressants and selective serotonin reuptake inhibitors or selective norepinephrine reuptake inhibitors. We are also aware that branded or generic stimulants may be prescribed off-label for treatment of EDS in narcolepsy. Wake-promoting agents modafinil and armodafinil, including both branded and generic equivalents, are approved for the treatment of EDS in narcolepsy and other conditions, and may be used in conjunction with or instead of Xywav or Xyrem.

- *Epidiolex*. Patients in the U.S. suffering from seizures associated with DS, LGS or TSC are treated with a variety of FDA-approved products, including clobazam, clonazepam, valproate, lamotrigine, levetiracetam, rufinamide, topiramate, ethosuximide, and zonisamide. FDA approved Zogenix, Inc.'s low-dose fenfluramine in DS in June 2020, and for LGS in March 2022. In March 2022, UCB S.A. announced that it had completed its acquisition of Zogenix. FDA approved Marinus Pharmaceuticals, Inc.'s ganaxolone for the treatment of seizures associated with cyclin-dependent kinase-like 5 deficiency disorder in March 2022. Ovid Therapeutics Inc./Takeda Pharmaceutical Company Limited, Eisai Company Limited and H Lundbeck A/S are developing therapies for treating Developmental and Epileptic Encephalopathies (includes DS and LGS). Stiripentol has been approved in Europe for several years to treat DS and was approved in 2018 by FDA. Harmony Biosciences is developing a topical formulation of CBD for which it is working with FDA on a path forward on CONNECT-FX data for Zylgel in Fragile X syndrome. There are a number of public and private companies in various stages of developing genetic therapies for DS, including Stoke Therapeutics, Inc., which has an antisense oligonucleotide, STK-001, in clinical trials.

In addition, there are non-FDA approved CBD preparations being made available from companies in the medical marijuana industry, which might attempt to compete with Epidiolex. While federal law prohibits the sale and distribution of most marijuana products not approved or authorized by FDA, the vast majority of states and the

District of Columbia have legalized either CBD or marijuana for either recreational or medical use, or both. Under the U.S. Farm Bill, enacted in late 2018, certain extracts and other material derived from cannabis are no longer controlled under the CSA. However, the marketing of such products as a food, dietary supplement, or for medical purposes remains subject to FDA requirements. With respect to the marketing of CBD as a food or dietary supplement, in January 2023 FDA concluded that the existing regulatory frameworks for foods and supplements were not appropriate for CBD products and denied three citizen petitions that had asked the agency to conduct rulemaking to allow the marketing of CBD products as dietary supplements. In addition, Congressional efforts related to legalization of marijuana continue. Although our business is distinct from that of entities marketing FDA-unapproved marijuana and CBD-containing dietary supplements, future legislation or federal government action authorizing the sale, distribution, use, and insurance reimbursement of non-FDA approved marijuana or CBD products could increase competition for and adversely affect our ability to generate sales of Epidiolex and our cannabinoid product candidates.

We are aware of exploratory research into the effects of tetrahydrocannabinol, often referred to as THC, and CBD drug formulations; discovery research within the pharmaceutical industry into synthetic agonists and antagonists of CB1 and CB2 receptors; companies that supply synthetic cannabinoids and cannabis extracts to researchers for pre-clinical and clinical investigation; and various companies that cultivate cannabis plants with a view to supplying herbal cannabis or nonpharmaceutical cannabis-based formulations to patients. These activities have not been approved by FDA but may in the future compete with our products.

Moreover, we expect that Epidiolex will face competition from generic products in the future. In November and December 2022, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex (cannabidiol) oral solution. In January 2023, we filed patent infringement suits against these ANDA filers. For a description of this litigation, see “*Epidiolex Patent Litigation*” in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. As a result of these lawsuits, we expect that a stay of approval of up to 30 months will be imposed by FDA on these ANDA filers.

- *Zepzelca*. Zepzelca faces competition from topotecan, which is also an approved treatment in second line SCLC in the U.S., as well as other regimens for relapsed SCLC currently recommended in compendia guidelines, including rechallenge with first line platinum chemotherapy. There are also a number of products and immunotherapies for the treatment of second line SCLC in various phases of development, including Amgen Inc.’s tarlatamab, which was approved for use in the U.S. in May 2024. Moreover, we expect that Zepzelca will face competition from generic products in the future. In July and August 2024, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Zepzelca (lurbinectedin). In September 2024, we filed patent infringement suits against these ANDA filers. For a description of this litigation, see “*Zepzelca Patent Litigation*” in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. As a result of these lawsuits, we expect that a stay of approval of up to 30 months will be imposed by FDA on these ANDA filers.
- *Rylaze*. Rylaze may face competition from Erwinaze in the future. Erwinaze was previously approved and commercialized by us as a treatment for ALL patients with hypersensitivity to *E. coli*-derived asparaginase. In April 2020, PBL granted Clinigen a global license for Erwinaze. However, in December 2021, Clinigen announced that FDA issued a complete response letter to PBL’s BLA for Erwinaze, indicating that the BLA cannot be approved in its current form. Outside of the U.S., Enrylaze faces competition from Erwinaze. Rylaze may also face competition from other companies who have developed or are developing new treatments for ALL. In addition, some new asparaginase treatments could reduce the rate of hypersensitivity in patients with ALL, and new treatment protocols are being developed and approved for ALL that may not include asparaginase-containing regimens, including some for the treatment of relapsed or refractory ALL patients.
- *Vyxeos*. With respect to Vyxeos, there are a number of alternative established therapies in AML. A key consideration in the treatment of AML patients is the patient’s suitability for chemotherapy. The AML patient population studied in the Vyxeos Phase 3 clinical trial supporting our NDA included 60-75 year old fit patients, or those deemed able to tolerate intensive induction chemotherapy. Prior to Vyxeos, the most widely recognized option for the treatment of newly-diagnosed t-AML and AML-MRC in fit patients was cytarabine in combination with daunorubicin, known as 7+3, which is still used today in this population, along with other intensive chemotherapy regimens, particularly in patients under the age of 60. Also, since Vyxeos was approved, several other products have been approved by FDA or are in development as treatment options for newly diagnosed AML patients eligible for intensive chemotherapy, such as targeted agents (e.g. midostaurin, enasidenib and ivosidenib), immunotherapies (e.g., gemtuzumab ozogamicin and chimeric antigen receptor T-cell therapy), and agents disrupting leukemia cell survival (e.g., glasdegib). We are also aware of the increasing use of venetoclax combined with either a hypomethylating

agent or low-dose cytarabine, a treatment approved by FDA in newly diagnosed AML patients who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. With ongoing trends in the U.S. towards lower-intensity treatments and away from intensive chemotherapy regimens for AML, we note increasing competition from other therapeutic options as we continue to educate providers on the clinical benefits of Vyxeos in appropriate patients.

- *Defitelio*. Defitelio is the first and only approved treatment for patients with VOD, sVOD, or VOD with renal or pulmonary dysfunction following HSCT by regulatory authorities in the U.S., Europe, Japan and other markets. Utilization of Defitelio is in part driven by evolving treatment practices in HSCT. While there is currently no direct competition to Defitelio to treat severe VOD, changes in the types of conditioning regimens used as part of HSCT may affect the incidence of VOD diagnosis and demand for Defitelio. In December 2024, FDA accepted an ANDA for a generic version of Defitelio (defibrotide sodium). We have yet to receive notice of this ANDA filing.
- *Zihera*. Zihera faces competition from generic chemotherapies, including cisplatin/gemcitabine rechallenge, and other HER2 directed therapies, including Enhertu and trastuzumab.

An important part of our corporate strategy is to build a diversified product pipeline, including by acquiring or in-licensing and developing, or partnering to license and develop, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Our ability to continue to grow our product portfolio requires that we compete successfully with other pharmaceutical companies, many of which may have substantially greater financial sales and marketing resources, to acquire or in-license products and product candidates.

Customers

In the U.S., Xywav and Xyrem are sold to one certified specialty pharmacy, ESSDS, that ships Xywav and Xyrem directly to patients. Also in the U.S., Epidiolex is sold to specialty pharmacies, wholesalers and specialty distributors. Defitelio is sold to hospital customers through subsidiary specialty distributors of McKesson. Zepzelca, Rylaze, Vyxeos and Zihera are sold to customers through subsidiary specialty distributors of McKesson, Cencora, and Cardinal. We have distribution services agreements made in the ordinary course of business with McKesson, Cencora and Cardinal and a pharmacy services agreement with ESSDS. For more information regarding our relationship with ESSDS, see “Business—Our Commercialized Products—Xywav and Xyrem REMS” in this Part I, Item 1. Purchases are made on a purchase order basis.

In certain countries in Europe, Defitelio and Vyxeos are sold pursuant to marketing authorizations. We distribute these products through Durbin PLC, a U.K.-based wholesaler and distributor, and O&M Movianto Nederland BV, our centralized European logistics services provider, to hospitals and local wholesalers in Europe where we market these products directly and, in other markets in Europe and elsewhere where we do not market these products directly, to local distributors and wholesalers. In certain countries in Europe, Epidiolex is sold pursuant to marketing authorizations. We distribute Epidiolex through a variety of wholesalers and distributors. In countries where there is no marketing authorization, Epidiolex is available pursuant to named patient programs, temporary use authorizations or similar authorizations in accordance with local regulations controlling the medical use of unapproved products.

We commercialize and distribute Xyrem in Canada for the treatment of cataplexy in patients with narcolepsy. Xyrem is also sold in certain countries outside the U.S. and Canada by UCB under the UCB license. In July 2024, the parties agreed to terminate the UCB license. UCB has up to two years from the execution of the termination agreement to withdraw the marketing authorization for Xyrem in all applicable territories.

Manufacturing

We have a manufacturing and development facility in Athlone, Ireland where we manufacture Xywav and Xyrem, a manufacturing and development facility in Kent Science Park, U.K. where we produce Epidiolex/Epidyolex, and a manufacturing plant in Villa Guardia, Italy where we produce defibrotide drug substance. We currently do not have our own commercial manufacturing or packaging capability for our other products, product candidates or their APIs. As a result, our ability to develop and supply products in a timely and competitive manner depends on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products.

Marketed Products

Xywav. Xywav is manufactured at our Athlone facility. Xywav, like Xyrem, is a Schedule III controlled substance in the U.S. The API of Xywav are the calcium, magnesium, potassium and sodium salts of gamma-hydroxybutyric acid (as gamma-hydroxybutyric acid is the API for Xyrem), which are Schedule I controlled substances in the U.S. As a result, Xywav and Xyrem are subject to regulation by the DEA under the CSA, and its manufacturing and distribution are highly restricted. Quotas from the DEA are required in order to manufacture or procure calcium, magnesium, potassium and sodium salts of gamma-hydroxybutyric acid in the U.S. For information related to DEA quota requirements, see “Business—Government

Regulation—Other Post-Approval Pharmaceutical Product Regulation—Controlled Substance Regulations* in this Part I, Item 1.

Xyrem. Xyrem is manufactured by us in our Athlone facility and by Patheon under the Patheon Agreement entered into with Patheon in 2015. We manufacture Xyrem in our Athlone facility for most of our U.S. commercial supply and rely on Patheon to supply Xyrem for other markets, though we are not required to purchase Xyrem exclusively from Patheon. The current term of the Patheon Agreement will expire in December 2026, subject to further automatic two-yearly extensions if Patheon is then providing manufacturing services for any product, unless either party provides prior notice of termination. In addition, we may terminate the Patheon Agreement for any reason upon 12 months' prior written notice.

Siegfried supply sodium oxybate, the API of Xyrem, to Patheon and our Athlone facility. Although Siegfried has been our only supplier of sodium oxybate since 2012, we have the right to purchase a portion of our worldwide requirements of sodium oxybate from other suppliers. The agreement with Siegfried expires in April 2027, subject to automatic three-year extensions until either party provides advance notice of its intent to terminate the agreement. During the term of the agreement and, under certain circumstances for 18 months after the agreement terminates, Siegfried is not permitted to manufacture sodium oxybate for any other company.

Epidiolex. Epidiolex/Epidyolex is manufactured by us in our Kent Science Park facility in the U.K. Epidiolex is a pharmaceutical formulation comprising highly purified plant-derived CBD. We cultivate our cannabinoid plants in the U.K. under highly controlled and standardized conditions.

Zepzelca. Zepzelca is manufactured by Simtra. The current term of the agreement with Simtra will expire in December 2025 and will then be subject to automatic two-year extensions, unless either party provides advance notice of its intent to terminate the agreement. PharmaMar retains manufacturing rights for the API for U.S. and Canadian commercial supply of Zepzelca.

Rylaze. Rylaze is currently manufactured by Patheon, and the API of Rylaze is manufactured by AGC Biologics A/S. The initial term of the agreement with Patheon will expire in December 2025 and will then be subject to automatic two-year extensions, unless either party provides advance notice of its intent to terminate the agreement. The initial term of the agreement with AGC Biologics A/S will expire in October 2026 and will then be subject to automatic three-year extensions, unless either party provides advance notice of its intent to terminate the agreement.

Vyxeos. Vyxeos is manufactured by Simtra, which is a sole source supplier from a single site location, using our CombiPlex technology platform. CombiPlex products represent formulations with increased manufacturing complexities associated with producing drug delivery vehicles encapsulating two or more drugs that are maintained at a fixed ratio and, in the case of Vyxeos, two drugs that are co-encapsulated in a freeze-dried liposomal format. Our manufacturing agreement with Simtra expires in August 2025, subject to automatic three-year renewal terms, unless either party provides advance notice of its intent to terminate the agreement. While other contract manufacturers may be able to produce Vyxeos, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. The marketing authorization in the EU for Vyxeos also requires us to comply with certain manufacturing-related post-approval commitments.

Defitelio. We are our own sole supplier of, and we believe that we are currently the sole worldwide producer of, defibrotide API. We manufacture defibrotide API from porcine DNA in a single facility located in Villa Guardia, Italy. Patheon currently processes defibrotide API into its finished vial form under a specific product agreement entered into under a separate agreement with Patheon. Patheon is the sole provider of our commercial and clinical supply of Defitelio; however, we are not required to purchase Defitelio exclusively from Patheon. If Patheon does not or is not able to supply us with Defitelio for any reason, it may take time and resources to implement and execute the necessary technology transfer to another processor, and such delay could negatively impact our anticipated revenues from Defitelio and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

Zihera. Zihera is manufactured by WuXi Biologics (Hong Kong) Limited at their manufacturing site in WuXi, China. The initial term of the agreement with WuXi will expire in March 2029 and will then be subject to automatic three year extensions, unless either party provides advance notice of its intent to terminate the agreement. We have the right to appoint an alternate contract manufacturer at our discretion.

Product Candidates

For discussion of the challenges we face with respect to supply of our products and product candidates, see the risk factor under the heading “*Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects*” in Part I, Item 1A of this Annual Report on Form 10-K.

Patents and Proprietary Rights

We actively seek to patent, or to acquire or obtain licenses to third party patents, to protect our products and product candidates and related inventions and improvements that we consider important to our business. We own a portfolio of U.S. and ex-U.S. patents and patent applications and have licensed rights to a number of issued patents and patent applications. Our owned and licensed patents and patent applications cover or relate to our products and product candidates, including certain formulations, used to treat particular conditions, distribution methods and methods of administration, drug delivery technologies and delivery profiles and methods of making and use. Patents extend for varying periods according to the date of the patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The patent laws of ex-U.S. countries differ from those in U.S., and the degree of protection afforded by ex-U.S. patents may be different from the protection offered by U.S. patents. In addition to patents, our products and product candidates are in some instances protected by various regulatory exclusivities. For a description of those exclusivities and their regulatory background, see “Business—Government Regulation—Marketing Exclusivity—The Hatch-Waxman Act” in this Part I, Item 1.

The patents, patent applications and regulatory exclusivities that relate to our marketed products include:

- *Xywav*: We have 15 U.S. patents that relate to Xywav. These patents expire from 2033 to 2041. In addition, we have patent applications that relate to Xywav for use in additional indications that would, if issued, expire between 2040 and 2041. Xywav has been granted ODE by FDA to treat narcolepsy through January 2028 (inclusive of six months of pediatric exclusivity) and to treat IH through August 2028. Some of our Xywav patents have been subject to patent litigation with the companies who filed ANDAs seeking to market a generic version of Xywav. For example, we received notices in June 2021 and February 2023, that Lupin and Teva, respectively, filed ANDAs for generic versions of Xywav. For additional information on litigation involving these matters, see Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.
- *Xyrem*: We currently have seven issued patents in the U.S. relating to Xyrem listed in the Orange Book. Our patents relate to a DDI between Xyrem and divalproex sodium. In October 2018, due to FDA’s grant of pediatric exclusivity, an additional six months was added to the original expiration dates of all of our Orange Book-listed patents that existed at that time. As a result, our Orange Book-listed patents have periods of exclusivity between December 2022 (with an additional six months for pediatric exclusivity) and September 2033. Some of our Xyrem patents have been subject to patent litigation with the companies who filed ANDAs seeking to market a generic version of Xyrem, including challenge through the IPR procedures of the PTAB. The PTAB dismissed some of the IPR petitions. However, in July 2018, the United States Court of Appeals for the Federal Circuit upheld on appeal PTAB decisions finding that six patents associated with the Xywav and Xyrem REMS and three claims of a seventh REMS patent were unpatentable. As a result, we will not be able to enforce patents or claims that the PTAB found unpatentable. Although we have settled all patent litigation against the ten companies that filed ANDAs, additional companies may challenge our U.S. patents for Xyrem in the future. For a description of our Xyrem settlements, see the risk factor under the heading “The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products” in Part I, Item 1A of this Annual Report on Form 10-K. For additional information on litigation involving our Orange Book-listed patents, see “*Avadel Litigation*” in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

The European Patent Office issued a method of administration patent relating to the DDI between Xyrem and divalproex sodium that expires in 2034.

- *Epidiolex*: Our patent portfolio relating to the use of CBD in the treatment of epileptic encephalopathies includes 32 issued U.S. patents listed in the Orange Book. These patents claim the use of CBD for the treatment of convulsive, drop and atonic seizures associated with both LGS and DS, an oral composition of CBD, as well as the use of CBD in combination with clobazam, and the teaching that dose adjustment may be needed when concomitantly prescribed. The patents currently listed in the Orange Book will expire between 2035 and 2041. We have filed corresponding patent applications in many jurisdictions worldwide, including Europe, U.K., Canada, Japan, Mexico, Australia and New Zealand. The USPTO has granted two patents based on data that demonstrates that Epidiolex provides a benefit over synthetic CBD in an animal model of epilepsy, which will expire in 2039 and which are listed in the Orange Book. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027. Some of our Epidiolex patents have been subject to patent litigation with the companies who filed ANDAs seeking to market a generic version of Epidiolex. In November and December 2022, ten companies sent us notices that they had filed ANDAs seeking approval to market a generic version of Epidiolex. For additional information on litigation involving these matters, see Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

- *Zepzelca*. In December 2019, we entered into an exclusive license agreement with PharmaMar pursuant to which we obtained exclusive U.S. development and commercialization rights to Zepzelca. In October 2020, we entered into the amended license agreement which expanded our exclusive license to include rights to develop and commercialize Zepzelca in Canada. We have a portfolio of in-licensed U.S. and Canadian patents for lurbinectedin relating to compositions, methods of use, and processes. For example, one Orange Book listed U.S. patent (expiring in 2029, with granted patent term extension) covers a genus of compounds, including lurbinectedin, and use in treating various cancers. A request for extension (CSP) has also been filed in Canada. Zepzelca has also been granted ODE for the treatment of adults with metastatic SCLC with disease progression on or after platinum-based chemotherapy until 2027 and new chemical entity exclusivity until 2025 in the U.S. In July and August 2024, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Zepzelca (lurbinectedin). In September 2024, we filed patent infringement suits against these ANDA filers. For a description of this litigation, see “*Zepzelca Patent Litigation*” in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. As a result of these lawsuits, we expect that a stay of approval of up to 30 months will be imposed by FDA on these ANDA filers.
- *Rylaze*. In 2016, we obtained worldwide rights from Pfenex, including Pfenex’s patent rights relating to Rylaze, to develop and commercialize multiple early-stage hematology product candidates, including a license to two U.S. process patents relating to Rylaze, with respective expirations in 2026 and 2038. Pfenex has been acquired by Ligand. Rylaze has been granted orphan drug designation for the treatment of patients with ALL or LBL. We have two patent application families relating to dosing regimens. One covers the dosing regimen (25mg/m² intramuscularly every 48 hours), while the other covers various dosing regimens of interest. If issued, these would expire in 2040 and 2042, respectively. Another patent application relating to formulations of asparaginase would expire in 2042, if issued.
- *Vyxeos*. We have a portfolio of U.S. and ex-U.S. patents and patent applications for Vyxeos and the CombiPlex technology platform relating to various compositions and methods of making and use. These include seven U.S. patents covering Vyxeos compositions and methods of use expiring between 2025 and 2032 and two U.S. patents covering CombiPlex (which also cover Vyxeos) expiring in January 2027. These patents are listed in the Orange Book. FDA granted Vyxeos ODE for the treatment of adults with newly-diagnosed t-AML or AML-MRC, which expired in August 2024. In March 2021, FDA approved an expanded label for Vyxeos for the treatment of t-AML or AML-MRC in pediatric patients 1 year and older. In addition, Vyxeos was granted OME by the EC until August 2028, ten years from its EC approval for the treatment of adults with newly-diagnosed t-AML or AML-MRC. Vyxeos was approved by Health Canada for treatment of adults with newly diagnosed t-AML or AML-MRC in April 2021. Vyxeos was approved in March 2024 in Japan and designated as an orphan drug.
- *Defitelio*. The unique process of deriving defibrotide from porcine DNA is extensive and uses both chemical and biological processes that rely on complex characterization methods. We have U.S. and non-U.S. patents and patent applications relating to various compositions, methods of use and methods of characterization, with the issued patents expiring at various times between 2021 and 2035. Three U.S. patents are listed in the Orange Book. In December 2024, FDA accepted an ANDA for a generic version of Defitelio (defibrotide sodium). We have yet to receive notice of this ANDA filing. Defibrotide has also been granted orphan drug designation by the Korean Ministry of Food and Drug Safety to treat and prevent VOD, by the Commonwealth of Australia-Department of Health for the treatment of VOD and by the EC for the prevention of acute Graft-versus-Host Disease. We acquired the rights to defibrotide for the treatment and prevention of VOD in North America, Central America and South America from Sigma-Tau Pharmaceuticals, Inc. in 2014.
- *Ziibera*. In 2022, we obtained a license from Zymeworks BC Inc., which included rights to a portfolio of U.S. and ex-U.S. patents and patent applications, including compositions and methods of using Ziibera. The portfolio contains a U.S. composition of matter patent relating to Ziibera, which expires in 2034 (excluding any adjustments or extensions).

The patents and/or patent applications that relate to our product candidates include:

- *JZP815*. Through a collaboration agreement and an asset purchase agreement with Redx in 2019, we acquired a portfolio of U.S. and ex-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP815. The portfolio contains a U.S. composition of matter patent relating to JZP815, which expires in 2035 (excluding any adjustments or extensions).
- *JZP898*. Through a license agreement with Werewolf in 2022, we obtained a license to a portfolio of U.S. and ex-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP898. The portfolio contains a U.S. composition of matter patent relating to JZP898, which, if granted, expires in 2040 (excluding any adjustments or extensions).

- *Suvecaltamide (JZP385)*. Through the acquisition of Cavion in 2019, we obtained a portfolio of U.S. and ex-U.S. patents and patent applications, including rights relating to compositions and methods of using suvecaltamide. The portfolio includes a U.S. composition of matter patent relating to suvecaltamide, which expires in 2027, but which may be extended to 2032 depending on regulatory approval. A U.S. patent to the treatment of ET may provide supplemental protection to 2039.
- *JZP441*. Through a license agreement with Sumitomo in 2022, we obtained a license to a portfolio of U.S. and ex-U.S. patents and patent applications, including rights relating to compositions and methods of using JZP441. The portfolio contains a U.S. composition of matter patent relating to JZP441, which expires in 2040 (excluding any adjustments or extensions).

In addition, we have rights to a number of trademarks and service marks, and pending trademark and service mark applications, in the U.S. and elsewhere in the world to further protect the proprietary position of our products. For a discussion of the challenges we face in obtaining or maintaining patent and/or trade secret protection, see the risk factors under the heading “Risks Related to Our Intellectual Property” in Part I, Item 1A of this Annual Report on Form 10-K.

Government Regulation

As a global pharmaceutical company, our activities are subject to extensive regulation in the U.S., Europe and other countries where we do business. Regulatory requirements encompass the entire life cycle of pharmaceutical products, from research and development activities to marketing approval, manufacturing, labeling, packaging, adverse event and safety reporting, storage, advertising, promotion, sale, pricing and reimbursement, recordkeeping, distribution, importing and exporting. Regulations differ from country to country and are constantly evolving.

Testing and Approval of Pharmaceutical Products

We are not permitted to market a product in a country until we receive approval from the relevant regulatory authority, such as FDA in the U.S. and the EC or the competent authorities of the EU member states. An application for marketing approval must contain information generated by the applicant, also called a sponsor, demonstrating the quality, safety and efficacy of the product candidate, including data from preclinical and clinical trials, proposed product packaging and labeling and information pertaining to product formulation and the manufacture and analytical testing of the API and the finished product.

In the U.S., FDA reviews and, if warranted, approves applications for marketing approval. The process for obtaining marketing approval in the U.S. for a drug or biologic product candidate generally includes:

- conducting preclinical laboratory and animal testing and submitting the results to FDA in an IND application requesting approval to test the product candidate in human clinical trials;
- conducting adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate in the desired indication;
- submitting an NDA, sNDA, BLA or sBLA as appropriate, to FDA seeking approval for a specific indication; and
- completing inspections by FDA of the facilities where the product candidate is manufactured, analyzed and stored to demonstrate compliance with cGMP, and any requested FDA audits of the clinical trial sites that generated the data supporting the application.

Human clinical trials conducted before approval of a product generally proceed in three sequential phases, although the phases may overlap. In Phase 1, the initial introduction of the product candidate in humans, the product candidate is typically tested to assess metabolism, pharmacokinetics, pharmacological actions and tolerability, including side effects associated with increasing doses. Phase 2 usually involves clinical trials in a limited patient population to determine the effectiveness of the product candidate for a particular indication or indications, dosage tolerance and optimum dosage and to identify common adverse effects and safety risks. If a product candidate demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2, Phase 3 clinical trials are undertaken to obtain additional information about clinical efficacy and safety in a larger number of patients. Clinical trials must be conducted in accordance with specific protocols, as well as FDA requirements related to conducting the trials and recording and reporting the results, commonly referred to as good clinical practices, to ensure that the resulting data are credible and accurate and that the trial participants are adequately protected. FDA enforces good clinical practices through periodic inspections of trial sponsors, clinical investigators and trial sites.

Once an NDA, sNDA, BLA or sBLA has been compiled and submitted, FDA performs an initial review before it accepts the application for filing. FDA may refuse to file an application and/or request additional information before acceptance. Once accepted for filing, FDA begins an in-depth review of the application. Under the current goals and policies agreed to by FDA under the PDUFA for a new molecular entity, FDA has ten months from the filing decision in which to complete its initial

review of a standard application and respond to the applicant, and six months from the filing decision for a priority application. FDA does not always meet its PDUFA goal dates, and in certain circumstances, the PDUFA goal date may be extended.

FDA also has various programs, including Fast Track, Priority Review, Breakthrough Therapy and Accelerated Approval (Subpart H and E), RTOR pilot program, that are intended to expedite the process for reviewing certain applications and/or provide for approval on the basis of surrogate endpoints or restricted distribution. Generally, products may be eligible for one or more of these programs if they are intended for serious or life-threatening diseases or conditions, have potential to address unmet medical needs, or may provide meaningful benefit over existing treatments. For example, FDA granted Vyxeos Breakthrough Therapy and Fast Track designations and granted Priority Review with respect to our NDA for Vyxeos for the treatment of t-AML and AML-MRC that was approved in August 2017. In addition, a PRV may be used to obtain priority review by FDA for one of our future regulatory submissions. We used the PRV we acquired in May 2018 to obtain priority review for our Xywav sNDA for the treatment of IH, which was approved by FDA in August 2021. In June 2020, FDA granted Accelerated Approval to Zepzelca for relapsed SCLC. In December 2020, we initiated the submission of a BLA for Rylaze for ALL under the RTOR pilot program, which was approved by FDA in June 2021.

During its review of an application, FDA evaluates whether the product demonstrates the required level of safety and efficacy for the indication for which approval is sought and conducts the inspections and audits described above. FDA may also refer an application to an advisory committee, typically a panel of clinicians, for review, evaluation and a non-binding recommendation as to whether the application should be approved. When FDA completes its evaluation, it issues either an approval letter or a complete response letter. A complete response letter generally outlines what FDA considers to be the deficiencies in the application and may indicate that substantial additional testing or information is required prior to FDA approval of the product. If and when identified deficiencies have been addressed to FDA's satisfaction after a review of the resubmission of the application FDA will issue an approval letter.

Even if a product is approved, the approval may be subject to limitations based on FDA's interpretation of the data submitted in the application. For example, as a condition of approval, FDA may require the sponsor to agree to certain post-marketing requirements, such as conducting Phase 4, or post-approval, clinical trials to gain additional safety data or to document a clinical benefit in the case of products approved under Accelerated Approval regulations. FDA's approval of the NDA for Defitelio included a number of post-marketing commitments and requirements, including the requirement that we conduct a clinical trial to analyze the safety of defibrotide versus best supportive care in the prevention of VOD in adult and pediatric patients. For its approval of Vyxeos, FDA required that we conduct a safety study to characterize infusion-related reactions in patients treated with Vyxeos and a clinical trial to determine dosing to minimize toxicity in patients with moderate and severe renal impairment. Further, FDA granted Accelerated Approval to Zepzelca for relapsed SCLC based on data from a Phase 2 trial, which approval is contingent upon verification and description of clinical benefit in a post-marketing clinical trial.

In addition, if FDA determines that a REMS is necessary to ensure that the benefits of the product outweigh the risks, a sponsor may be required to include a proposed REMS (either as part of the application or after approval), which may include a patient package insert or a medication guide to provide information to consumers about the product's risks and benefits; a plan for communication to healthcare providers; or conditions on the product's prescribing or distribution referred to as elements to assure safe use. Xywav and Xyrem are required to have a REMS. For more discussion regarding the Xywav and Xyrem REMS, see the risk factors under the headings "*The distribution and sale of our oxybate products are subject to significant regulatory restrictions, including the requirements of a REMS, and these regulatory requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xywav and Xyrem*" and "Risks Related to Our Intellectual Property" in Part I, Item 1A of this Annual Report on Form 10-K.

The EU and many individual countries have regulatory structures similar to the U.S. for conducting preclinical and clinical testing and applying for marketing approval or authorization, although specifics may vary widely from country to country. Clinical trials in the EU must be conducted in accordance with the requirements of the EU Clinical Trials Regulation and applicable good clinical practice standards. In the EU, there are several procedures for requesting marketing authorization which can be more efficient than applying for authorization on a country-by-country basis. There is a "centralized" procedure allowing submission of a single marketing authorization application to EMA. If EMA issues a positive opinion, the EC will grant a centralized marketing authorization that is valid in all EU member states and three of the four European Free Trade Association countries (Iceland, Liechtenstein and Norway). The centralized procedure is mandatory for certain medicinal products, including orphan medicinal products and biotechnology-derived medicinal products, and optional for others. There is also a "decentralized" procedure allowing companies to file identical applications to several EU member states simultaneously for product candidates that have not yet been authorized in any EU member state and a "mutual recognition" procedure allowing companies that have a product already authorized in one EU member state to apply for that authorization to be recognized by the competent authorities in other EU member states. The U.K.'s withdrawal from the EU on January 31, 2020, commonly referred to as Brexit, has created uncertainty concerning the future relationship between the U.K. and the EU. Among the changes that have had a direct impact are that Great Britain (England, Scotland and Wales) is now treated as a third country. To mitigate the immediate impact of this in December 2020, the EU and U.K. reached an agreement in principle on

the framework for their future relationship, the EU-U.K. TCA. With regard to EU regulations, Northern Ireland continues to follow the EU regulatory rules. As part of the TCA, the EU and the U.K. recognize GMP, inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The TCA also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The U.K. has unilaterally agreed to accept EU batch testing and batch release; there is a list of approved countries for import into Great Britain, currently including EU and EEA countries, which require no import testing or U.K. “qualified person” release certification. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the U.K. must be retested and re-released when entering the EU market for commercial use. As regards marketing authorizations, Great Britain has introduced a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland, however, continues to be covered by the marketing authorizations granted by the EC.

The maximum timeframe for the evaluation of an application in the EU under the centralized procedure is 210 days, subject to certain exceptions and clock stops. An initial marketing authorization granted in the EU is valid for five years, with renewal subject to re-evaluation of the risk-benefit profile of the product. Once renewed, the authorization is usually valid for an unlimited period unless the national competent authority or the EC decides on justified grounds to proceed with one additional five-year renewal.

In the EU, if an applicant can demonstrate that comprehensive data on the efficacy and safety of the product under normal conditions of use cannot be provided due to certain specified objective and verifiable reasons, products may be granted marketing authorization “under exceptional circumstances.” A marketing authorization granted under exceptional circumstances is valid for five years, subject to an annual reassessment of conditions imposed by the EC. The marketing authorization in the EU for Defitelio was granted under exceptional circumstances because it was not possible to obtain complete information about the product due to the rarity of the disease and because ethical considerations prevented conducting a study directly comparing Defitelio with best supportive care or a placebo. As a result, the marketing authorization requires us to comply with a number of post-marketing obligations, including obligations relating to the manufacture of the drug substance and finished product, the submission of data concerning patients treated with the product collected through a third-party patient registry and the establishment of a multi-center, multinational and prospective observational patient registry to investigate the long-term safety, health outcomes and patterns of utilization of Defitelio during normal use. We are in the process of conducting the post-authorization study in the EU to provide further data on long-term safety, health outcomes and patterns of utilization of Defitelio in normal use.

Similar to the use of REMS in the U.S. to ensure that the benefits of a product outweigh its risks, in the EU and other countries we are required and may, in the future in relation to new products, be required to agree to post-marketing obligations or conditions in the marketing authorization for our products, to include a patient package insert or a medication guide to provide information to consumers about the product’s risks and benefits, to implement a plan for communication to healthcare providers, and to impose restrictions on the product’s distribution. For example, the marketing authorization in the EU for Vyxeos requires us to comply with certain manufacturing-related post-approval commitments.

After approval, certain changes to the approved product, such as adding new indications, making certain manufacturing changes, modifying a REMS, or making certain additional labeling claims, are subject to further regulatory review and approval. Obtaining approval for a new indication generally requires that additional clinical studies be conducted to demonstrate that the product is safe and effective for the new intended use. Such regulatory reviews can result in denial or modification of the planned changes, or requirements to conduct additional tests or evaluations that can substantially delay or increase the cost of the planned changes.

Manufacture of Pharmaceutical Products

The manufacturing process for pharmaceutical products is highly regulated, and regulators may shut down manufacturing facilities that they believe do not comply with regulations. We and the third party suppliers of our products are subject to cGMP, which are extensive regulations governing manufacturing processes, stability testing, recordkeeping and quality standards as defined by FDA, the EC, EMA, competent authorities of EU member states and other regulatory authorities. FDA also periodically inspects manufacturing facilities and the sponsor’s and manufacturer’s records related to manufacturing, and assesses compliance with cGMP. Following such inspections, FDA may issue notices on Form FDA 483 and warning letters. In addition to Form FDA 483 notices and warning letters, failure to comply with the statutory and regulatory requirements may result in suspension of manufacturing, product seizure, withdrawal of the product from the market, administrative, civil and criminal penalties, among other enforcement remedies both in the U.S. and in non-U.S. countries.

In the EU, a manufacturing authorization is required to manufacture medicinal products, and the manufacturing authorization holder must comply with various requirements set out in applicable EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing products and their APIs, including APIs

manufactured outside of the EU with the intention of importing them into the EU. In addition to inspection reports, manufacturers and marketing authorization holders may be subject to civil, criminal or administrative sanctions, including suspension of manufacturing authorization, in cases of non-compliance with the EU or EU member states' requirements applicable to manufacturing.

Sales and Marketing of Pharmaceutical Products

Advertising and Promotional Activities

FDA regulates advertising and promotional activities for products in the U.S., requiring advertising, promotional materials and labeling to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. FDA actively investigates allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. FDA routinely issues informal and more formal communications such as untitled letters or warning letters interpreting its authority over these matters. While such communications may not be considered final agency decisions, many companies may decide not to contest the agency's interpretations so as to avoid disputes with FDA, even if they believe the claims they were making to be truthful, not misleading and otherwise lawful.

In the EU, the advertising and promotion of our products are subject to laws governing promotion of medicinal products, interactions with physicians, misleading and comparative advertising and unfair commercial practices. For example, applicable laws require that promotional materials and advertising in relation to medicinal products comply with the product's SmPC as approved by the competent authorities in connection with a marketing authorization approval. The SmPC is the document that provides information to physicians concerning the safe and effective use of the product. Promotional activity that does not comply with the SmPC is considered off-label and is prohibited in the EU. Other applicable laws at the EU level and in the individual EU member states also apply to the advertising and promotion of medicinal products, including laws that prohibit the direct-to-consumer advertising of prescription-only medicinal products and further limit or restrict the advertising and promotion of our products to the general public and to health care professionals. Violations of the rules governing the promotion of medicinal products in the EU could be penalized by administrative measures, fines and imprisonment.

Fraud and Abuse

We are also subject to numerous fraud and abuse laws and regulations globally. In the U.S., there are a variety of federal and state laws restricting certain marketing practices in the pharmaceutical industry pertaining to healthcare fraud and abuse, including anti-kickback laws and false claims laws. Our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws. The U.S. federal healthcare program Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving anything of value to induce (or in return for) the referral of business, including the purchase, recommendation or prescription of a particular drug reimbursable under Medicare, Medicaid or other federally financed healthcare programs. The statute has been interpreted to apply to arrangements between pharmaceutical companies on one hand and patients, prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common manufacturer business arrangements and activities from prosecution and administrative sanction, the exemptions and safe harbors are drawn narrowly and are subject to regulatory revision or changes in interpretation by the DOJ and the OIG. Practices or arrangements that involve remuneration may be subject to scrutiny if they do not qualify for an exemption or safe harbor. For example, in November 2020, the OIG issued a Special Fraud Alert to highlight certain inherent risks of remuneration related to speaker programs sponsored by drug and device companies, which may not in all circumstances qualify under either safe harbor or statutory exception protection. The Special Fraud Alert sent a clear signal that speaker programs will be subject to potentially heightened enforcement scrutiny, in particular for those programs with certain characteristics identified as risk factors by OIG, including meals exceeding modest value or where alcohol is made available; lack of substantive or new content presented; programs held at venues not conducive to the exchange of educational information; repeat attendees or attendees without a legitimate business interest; sales or marketing influence on speaker selection; and excessive speaker compensation. Violations of the federal Anti-Kickback Statute may be established without providing specific intent to violate the statute, and may be punishable by civil, criminal, and administrative fines and penalties, damages, imprisonment, and/or exclusion from participation in federal healthcare programs.

The federal civil False Claims Act prohibits, among other things, any person from knowingly presenting, or causing to be presented, a false or fraudulent claim for payment of federal funds, or knowingly making, or causing to be made, a false record or statement to get a false claim paid. A claim resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim. The False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of themselves and the federal government alleging violations of the statute and to share in any monetary recovery. Violations of the False Claims Act may result in significant financial penalties (including mandatory penalties on a per claim or statement basis), treble damages and exclusion from participation in federal health care programs.

Pharmaceutical companies are subject to other federal false claim and statements laws, some of which extend to non-government health benefit programs. For example, the healthcare fraud provisions under HIPAA impose criminal liability for,

among other things, knowingly and willfully executing, or attempting to execute, a scheme to defraud any health care benefit program, including private third party payors, or falsifying or covering up a material fact or making any materially false or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services. Violations of HIPAA fraud provisions may result in criminal, civil and administrative penalties, fines and damages, including exclusion from participation in federal healthcare programs.

The majority of individual states also have statutes or regulations similar to the federal Anti-Kickback Statute and the False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Other states restrict whether and when pharmaceutical companies may provide meals to health care professionals or engage in other marketing-related activities, and certain states and cities require identification or licensing of sales representatives.

Other Post-Approval Pharmaceutical Product Regulation

Safety Reporting/Pharmacovigilance

FDA, EMA and other governmental authorities track information on side effects and adverse events reported during clinical studies and after marketing approval. We are required to file periodic safety update reports with the authorities concerning adverse events. If, upon review, an authority determines that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing, require post-approval safety studies, require a labor intensive collection of data regarding the risks and benefits of marketed products and ongoing assessments of those risks and benefits and/or require or conduct other actions, potentially including withdrawal or suspension of the product from the market. For example, if EMA has concerns that the risk-benefit profile of a product has changed, it can, following an investigation procedure, adopt an opinion advising that the existing marketing authorization for the product be varied or suspended and requiring the marketing authorization holder to conduct post-authorization safety studies. The opinion is then submitted for approval by the EC. Also, from time to time, FDA issues drug safety communications on its adverse event reporting system based on its review of reported adverse events.

FDA and the competent authorities of the EU member states on behalf of EMA also periodically inspect our records related to safety reporting. Following such inspections, FDA may issue notices on FDA Form 483 and warning letters that could cause us to modify certain activities. An FDA Form 483 notice, if issued, can list conditions FDA investigators believe may have violated relevant FDA regulations or guidance. Failure to adequately and promptly correct the observation(s) can result in a warning letter or other regulatory enforcement action. Similarly, EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps. Non-compliance can lead to the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Sunshine Act and Transparency Laws

The Sunshine provisions require tracking of payments and transfers of value to physicians and teaching hospitals and ownership interests held by physicians and their families, and reporting to the federal government and public disclosure of these data. Since 2022, reporting has been required of information regarding payments and transfers of value provided to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse-midwives. A number of states now require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to healthcare providers in the states. Government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products, which is prohibited in the EU, is governed by the national anti-bribery laws of the EU member states, as described below in "Business—Government Regulation—Anti-Corruption Legislation" in this Part I, Item I. Violation of these laws could result in substantial fines and imprisonment. Certain EU member states, or industry codes of conduct, require that payments made to physicians be publicly disclosed. Moreover, agreements with physicians must often be the subject of prior notification and approval by the physician's employer, his/her competent professional organization, and/or the competent authorities of the individual EU member states. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Controlled Substance Regulations

A drug product approved by FDA may be subject to scheduling as a controlled substance under the CSA depending on the drug's potential for abuse. Controlled substances that are pharmaceutical products are subject to a high degree of regulation under the CSA, which establishes, among other things, certain registration, manufacturing quotas, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five

schedules. Schedule I substances have a high potential for abuse, have no currently “accepted medical use” in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. may be classified as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse. The API of Xywav and Xyrem, oxybate salts, are regulated by the DEA as Schedule I controlled substances, and Xywav and Xyrem drug products are regulated as Schedule III controlled substances. Certain product candidates we are developing contain controlled substances as defined in the CSA. Drug products approved by FDA that contain cannabis or cannabis extracts may be controlled substances and will be rescheduled to Schedules II-V after approval or, like Epidiolex, removed completely from the schedules by operation of other laws.

The DEA limits the quantity of certain Schedule I and II controlled substances that may be manufactured and procured in the U.S. in any given calendar year through a quota system and, as a result, quotas from the DEA are required in order to manufacture and procure oxybate salts in the U.S. Accordingly, we require DEA quotas for Siegfried, our U.S. based sodium oxybate supplier, to manufacture sodium oxybate and for Patheon, our U.S.-based Xyrem supplier, to procure sodium oxybate from Siegfried in order to manufacture and supply us with Xyrem drug product. We also require DEA quotas for Patheon to manufacture and procure the API of Xywav oxybate salt. Xywav and Xyrem manufactured at our plant in Ireland enter the U.S. as Schedule III drugs and therefore do not require a DEA manufacturing or procurement quota.

As Schedule III drugs, Xywav and Xyrem are also subject to DEA and state regulations relating to the importation, manufacturing, storage, distribution and physician prescription procedures, including limitations on prescription refills. In addition, the third parties who perform our clinical and commercial manufacturing, distribution, dispensing and clinical studies for Xywav and Xyrem are required to maintain necessary DEA registrations and state licenses. The DEA periodically inspects facilities for compliance with its rules and regulations.

Other Regulations

There are many other requirements and restrictions in the U.S. and elsewhere imposed on pharmaceutical companies and their activities, including those related to the posting of information relating to clinical studies and their outcomes, the export and importation of products, required authorizations for distributors, the identification or licensing of sales representatives, restrictions on the ability of manufacturers to offer co-pay support to patients for certain prescription drugs, implementation of required compliance programs or marketing codes of conduct, protection of the environment, taxation and work safety. Non-compliance with such requirements may result in civil, criminal or administrative sanctions.

Anti-Corruption Legislation

Our business activities outside of the U.S. are subject to the FCPA, and similar anti-bribery or anti-corruption laws, regulations, industry self-regulation codes of conduct and physicians’ codes of professional conduct or rules of other countries in which we operate, including the U.K. Bribery Act. The FCPA and similar anti-corruption laws in other countries generally prohibit the offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to U.S. or non-U.S. government officials in order to improperly influence any act or decision, secure an improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. The U.K. Bribery Act prohibits giving, offering, or promising bribes to any person, including U.K. and non-U.K. government officials and private persons, as well as requesting, agreeing to receive, or accepting bribes from any person. In addition, under the U.K. Bribery Act, companies that carry on a business or part of a business in the U.K. may be held liable for bribes given, offered or promised to any person, including U.K. and non-U.K. government officials and private persons in any country, by employees and persons associated with the company in order to obtain or retain business or a business advantage for the company. Liability is strict, with no element of a corrupt state of mind, but a defense of having in place adequate procedures designed to prevent bribery is available under the U.K. Bribery Act and certain other laws; under the FCPA, it might be considered as a mitigating factor.

As described above, our business is heavily regulated and therefore involves significant interaction with government officials in many countries. Additionally, in certain countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to the FCPA, the U.K. Bribery Act and similar laws. Recently the SEC, and the DOJ have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd-Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We engage in ongoing efforts designed to ensure our compliance with these laws, including conducting due diligence of our business partners, requiring training of our employees on FCPA requirements, and implementing and maintaining policies, procedures, and internal controls to ensure compliance with the FCPA and similar laws. However, there is no certainty that all employees and third party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In

particular, we do not control the actions of our suppliers and other third party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, disgorgement of past profits, and could cause disruption to our business, including through procurement bans or similar administrative actions. It is possible that an adverse outcome in an FCPA action could materially affect our consolidated results of operations, liquidity, and financial position and result in parallel civil litigation such as securities class actions and shareholder derivative suits.

Data Protection and Privacy

We are subject to data protection and privacy laws and regulations globally, which restrict the processing of personal data. The legislative and regulatory landscape for privacy and data security continues to evolve with an increased attention in countries globally that could potentially affect our business. In particular, we are subject to the EU General Data Protection Regulation, which imposes penalties up to 4% of annual global revenue, the California Consumer Privacy Act of 2018, as amended by the California Consumer Privacy Rights Act, and numerous other federal, state, national and international laws and regulations that govern the privacy and security of the personal data we collect and maintain. These laws and regulations applicable to our business, increase potential enforcement and litigation activity. In order to manage these evolving risks, we have adopted a global privacy program that governs the processing of personal data across our business.

Marketing Exclusivity

The Hatch-Waxman Act

The marketing approval process described above for the U.S. is premised on the applicant being the owner of, or having obtained a right of reference to, all of the data required to prove the safety and effectiveness of a drug product. This type of marketing application, sometimes referred to as a “full” or “stand-alone” NDA, is governed by Section 505(b)(1) of the FDCA. A Section 505(b)(1) NDA contains full reports of investigations of safety and effectiveness, which includes the results of preclinical and clinical trials, together with detailed information on the manufacture and composition of the product, in addition to other information. As an alternative, the Hatch-Waxman Act provides two abbreviated approval pathways for certain drug products.

The first path, under Section 505(b)(2) of the FDCA, usually is used for the approval of a product that is similar, but not identical, to a previously-approved brand-name product, referred to as the RLD. Under this path, the applicant is permitted to rely to some degree on FDA’s finding that the RLD is safe and effective and must submit its own product-specific data on safety and effectiveness only to the extent necessary to bridge the differences between the products. The second abbreviated path established under the Hatch-Waxman Act is for the approval of generic drugs. Section 505(j) of the FDCA permits the submission of an ANDA for a generic version of an approved, brand-name drug. Generally, an ANDA must contain data and information showing that the proposed generic product and the RLD (i) have the same active ingredient, in the same strength and dosage form, to be delivered via the same route of administration, (ii) are intended for the same uses, and (iii) are bioequivalent. This data and information are provided instead of data and information independently demonstrating the proposed generic product’s safety and effectiveness.

The Hatch-Waxman Act requires an ANDA or a Section 505(b)(2) NDA applicant to certify that there are no patents listed for that product in the Orange Book, or that for each Orange Book-listed patent either the listed patent has expired, the listed patent will expire on a particular date and approval is sought after patent expiration, or the listed patent is invalid or will not be infringed by the manufacture, use or sale of the new product. A certification that approval is sought after patent expiration is called a “Paragraph III Certification.” A certification that the new product will not infringe the RLD’s Orange Book-listed patents, or that such patents are invalid, is called a “Paragraph IV Certification.” If a relevant patent covers an approved method of use, an ANDA or Section 505(b)(2) NDA applicant can also file a statement, called, in the case of an ANDA, a “section viii statement,” that the application does not seek approval of the method of use covered by the listed patent. With such a statement, the applicant must “carve out” the protected method of use (typically an indication and related material) from the proposed product’s labeling. If the applicant makes a Paragraph III Certification, the ANDA or the Section 505(b)(2) NDA will not be approved until the listed patents claiming the RLD have expired.

If the applicant has provided a Paragraph IV Certification to FDA, the applicant must also send a notice of that certification to the NDA holder and the relevant patent holders once FDA accepts the ANDA or the Section 505(b)(2) NDA for filing. The NDA and patent holders then have 45 days to initiate a patent infringement lawsuit. Filing the lawsuit triggers an automatic stay on FDA’s approval of the ANDA or the Section 505(b)(2) NDA until the earliest of 30 months after the NDA holder’s receipt of the notice of Paragraph IV Certification, expiration of the patent, certain settlements of the lawsuit, or a decision in the infringement case that is favorable to the applicant. FDA may issue tentative approval of an application if the application meets all conditions for approval but cannot receive effective approval because the 30-month stay or another period of regulatory exclusivity has not expired. If an ANDA or Section 505(b)(2) NDA is approved before conclusion of any relevant patent litigation, the applicant can choose to launch the product, but does so “at risk” of being liable for damages, and potentially treble damages, if the RLD sponsor or patent holder ultimately prevails in patent litigation.

Under the Hatch-Waxman Act, newly approved drugs and indications may benefit from statutory periods of non-patent marketing exclusivity that can potentially delay review or approval of an ANDA or Section 505(b)(2) application. For example, the Hatch-Waxman Act provides five-year marketing exclusivity to the first applicant to gain approval of an NDA for a new chemical entity, meaning a drug containing an active moiety that FDA has not previously approved. During this period, FDA cannot accept for review an ANDA or a Section 505(b)(2) NDA for a product containing the same moiety, except that an application containing a Paragraph IV Certification may be submitted after four years, which may trigger the litigation and stay described above. The Hatch-Waxman Act also provides three years of marketing exclusivity with the approval of an NDA, including a Section 505(b)(2) NDA, for a product containing a previously-approved moiety but that incorporates a change (such as a new indication, dosage form or strength) from an approved product with the same moiety, if the change required clinical data from new investigations that were conducted or sponsored by the applicant. This three-year exclusivity does not preclude submission of the ANDA or Section 505(b)(2) NDA for such a product, but prevents FDA from giving final approval to such product.

The Hatch-Waxman Act also permits a patent term extension of up to five years (but not beyond 14 years from the date of approval) for an NDA, including a Section 505(b)(2) NDA, that is approved for a product that contains an active ingredient that has not previously been approved. The extension, which compensates for patent term lost during product development and FDA regulatory review process, is generally equal to the sum of one-half the time between the effective date of an IND application and the submission date of an NDA, and all of the time between the submission date of an NDA and the approval of that application. It is available for only one patent for a given product, and it must be a patent that claims the product or a method of using or manufacturing the product. The USPTO, in consultation with FDA, reviews and approves applications for patent term extension.

In the EU, innovative medicinal products that are subject to marketing authorization on the basis of a full dossier qualify for eight years' data exclusivity upon marketing authorization and an additional two years' market exclusivity. Data exclusivity prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product, after which a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced. However, the generic product or biosimilar products cannot be marketed in the EU for a further two years thereafter. The overall ten-year period may be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. In April 2023, the European Commission proposed the "Pharmaceutical Package", which aims to revise and replace existing pharmaceutical legislation to enhance the availability, accessibility, and affordability of medicinal products across the EU. This package includes a proposal for a new directive and a new regulation that would replace the current pharmaceutical legislation in the EU. Among others, the standard data protection period is proposed to decrease from eight to six years but would allow extensions of up to 12 years if specific conditions are met. As of January 2025, the legislative process is ongoing. Once an agreement is reached between the Council and the European Parliament, the legislation will be formally adopted and published. Its adoption is likely to occur in 2026, with implementation following thereafter.

Orphan Drug and Other Exclusivities

Some jurisdictions, including the U.S., may designate drugs or biologics for relatively small patient populations as orphan drugs. FDA grants orphan drug designation to drugs or biologics intended to treat a rare disease or condition, which is one that affects fewer than 200,000 individuals in the U.S., or more than 200,000 individuals, but for which there is no reasonable expectation that the cost of developing the product and making it available in the U.S. for the disease or condition will be recovered from U.S. sales of the product. Orphan drug designation does not shorten the duration of the regulatory review process or lower the approval standards, but can provide important benefits, including consultation with FDA. If a product is approved for its orphan designated use, it may be entitled to ODE, which blocks FDA from approving for seven years any other application for a product that is the same drug for the same indication. If there is a previously-approved product that is the same drug for the same indication, orphan drug designation requires the sponsor to provide a plausible hypothesis of clinical superiority over the approved product, whereas ODE requires the sponsor to actually demonstrate clinical superiority. Clinical superiority can be established by way of greater efficacy, greater safety, or making a major contribution to patient care. Additionally, a later product can be approved if the sponsor holding ODE consents, or cannot adequately supply the market. ODE does not prevent approval of another sponsor's application for different indications or uses of the same drug, or for different drugs for the same indication. Defibrotide was granted ODE by FDA to treat and prevent VOD until March 2023. Vyxeos was granted ODE by FDA for the treatment of AML until August 2024. Epidiolex has received ODE to treat seizures associated with LGS and DS through 2025 and TSC through 2027. In June 2021, FDA, recognized seven years of ODE for Xywav stating that Xywav is clinically superior to Xyrem by means of greater safety due to reduced chronic sodium burden. Xywav has been granted ODE by FDA to treat narcolepsy through January 2027 and to treat IH through August 2028. Rylaze has been granted ODE for the treatment of patients with ALL or LBL until 2028.

Biologic products approved under a BLA are subject to the BPCIA, which authorizes an abbreviated approval pathway for a biological product that is “biosimilar” to an already approved biologic, or reference product. The BPCIA provides periods of exclusivity that protect a reference product from competition by biosimilars. FDA may not accept a biosimilar application for review until four years after the date of first licensure of the reference product, and the biosimilar cannot be licensed until 12 years after the reference product was first licensed.

Under certain circumstances, the exclusivity periods applicable to drugs and biologics and the patent-related protections applicable to drugs may be eligible for a six-month extension if the sponsor submits pediatric data that fairly respond to a written request from FDA for such data. This exclusivity may be granted even if the data does not support a pediatric indication. We consider seeking pediatric exclusivity for our products whenever appropriate. For example, in response to a written request from FDA, we conducted a Phase 3 clinical trial to assess the safety and efficacy of Xyrem in children and adolescents aged seven to 17 who have narcolepsy with cataplexy, and submitted study results in a supplement to the Xyrem NDA, seeking approval for this indication. In October 2018, FDA approved the sNDA and notified us that we had been granted pediatric exclusivity, extending by six months the preclusive effect of our Orange Book-listed patents for Xyrem, as well as the three-year regulatory exclusivity period granted to the Xyrem pediatric indication because of the clinical studies that were necessary for approval of the sNDA.

In the EU, orphan designation may be granted to products that can be used to treat life-threatening diseases or chronically debilitating conditions with an incidence of no more than five in 10,000 people or that, for economic reasons, would be unlikely to be developed without incentives. Orphan designated medicinal products are entitled to a range of benefits during the development and regulatory review process and ten years of OME in all EU member states upon approval. As in the U.S., a similar medicinal product with the same orphan indication may be approved, notwithstanding OME, if the exclusivity holder gives consent or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if the similar product is deemed safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of OME granted in relation to the original orphan medicinal product may, in addition, be reduced to six years if it can be demonstrated, on the basis of available evidence, that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity. Defibrotide was granted orphan drug designation by the EC for the treatment of VOD and prevention of GvHD until October 2023, by the Korean Ministry of Food and Drug Safety to treat and prevent VOD, and by the Commonwealth of Australia-Department of Health for the treatment of VOD. Vyxeos has been granted OME by the EC until August 2028. Epidyolex has been granted OME for use as adjunct therapy of seizures associated with DS and LGS until September 2029, and for use as adjunctive therapy of seizures associated with TSC until April 2031.

Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access

Pricing and Reimbursement

Successful commercialization of our products depends in significant part on adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicaid and Medicare programs in the U.S.), managed care organizations and private health insurers. Third party payors decide which drugs will be reimbursed and establish reimbursement and co-pay levels and conditions for reimbursement. Third party payors are increasingly challenging the prices charged for medical products and services by examining their cost effectiveness, as demonstrated in pharmacoeconomic and/or clinical studies, in addition to their safety and efficacy. In some cases, for example, third party payors try to encourage the use of less expensive products, when available, through their prescription benefits coverage and reimbursement, co-pay and prior authorization policies. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third party payors may require prior approval before covering a specific product, or may require patients and health care providers to try other covered products first. Third party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication. For certain categories of products, third party payors, principally through contracted PBMs negotiate rebates with drug manufacturers for inclusion of products on their formularies in specific positions or coverage criteria. Beginning in the third quarter of 2019, we have been entering into agreements with certain PBMs or similar organizations to provide rebates for our products where coverage was provided and products were listed in certain formulary positions, among other conditions.

Medicaid is a joint federal and state program that is administered by the states for low-income and disabled beneficiaries. Medicare is a federal program that is administered by the federal government covering individuals age 65 and over as well as those with certain disabilities. Medicare Part B pays physicians who administer our products. Under the Medicaid Drug Rebate Program, as a condition of having federal funds made available to the states for our drugs under Medicaid and Medicare Part B, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program. Medicaid rebates are based on pricing data we report on a monthly and quarterly basis to the CMS, the federal agency that administers Medicare and Medicaid, including the Medicaid Drug Rebate Program. These data include the average manufacturer price and, in the case of innovator products, the best price

for each drug which, in general, represents the lowest price available from the manufacturer to any entity in the U.S. in any pricing structure, calculated to include all applicable sales and associated rebates, discounts and other price concessions. If we become aware that our reporting for a prior quarter was incorrect, or has changed as a result of recalculation of the pricing data, we are obligated to resubmit the corrected data for up to three years after those data originally were due. We are required to provide ASP information for certain of our products to CMS on a quarterly basis. The ASP is calculated based on a statutorily defined formula as well as regulations and interpretations of the statute by CMS. This information may be used to compute Medicare payment rates, with rates for Medicare Part B drugs outside the hospital outpatient setting and in the hospital outpatient setting consisting of ASP plus a specified percentage.

Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the 340B program, in order for federal funds to be available for the manufacturer's drugs under Medicaid and Medicare Part B. The 340B program, which is administered by the HRSA requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered drugs used in an outpatient setting. These 340B covered entities include certain qualifying community health clinics, a variety of entities that receive health services grants from the Public Health Service, and multiple categories of hospitals, including children's hospitals, critical access hospitals, free standing cancer hospitals and hospitals that serve a disproportionate share of low-income patients. The 340B ceiling price is calculated using a statutory formula, which is based on the average manufacturer price and rebate amount for the covered outpatient drug as calculated under the Medicaid Drug Rebate Program, and in general, products subject to Medicaid price reporting and rebate liability are also subject to the 340B ceiling price calculation and discount requirement. A regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities became effective on January 1, 2019. We also are required to report our 340B ceiling prices to HRSA on a quarterly basis and HRSA then publishes them to 340B covered entities. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in an inpatient setting.

A provision in The American Rescue Plan Act of 2021 eliminated, effective January 2024, the statutory cap on rebates drug manufacturers are required to pay under the Medicaid Drug Rebate Program. The elimination of the cap on rebates means that manufacturer discounts to Medicaid may rise beginning in 2024 and, in certain circumstances, rebates could exceed the amount that state Medicaid programs pay for the drug. This policy change will have the greatest impact on drugs whose prices have reached the 100 percent Average Manufacturer Price rebate cap. Further, the Inflation Reduction Act of 2022 among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs and a change in manufacturer liability under the program, which could negatively affect our business and financial condition.

Effective January 2023, a provision of the Infrastructure Investment and Jobs Act requires a manufacturer of single source drugs or biologicals in single-use packages or single dose containers to pay a refund on discarded amounts of drug under Medicare Part B where the discarded amount exceeds an applicable threshold.

In order to be eligible to have our products paid for with federal funds under the Medicaid and Medicare Part B programs and purchased by certain federal agencies and grantees, we also participate in the VA FSS pricing program. Under this program, we are obligated to make our products available for procurement on an FSS contract under which we must comply with standard government terms and conditions and charge a price to certain federal agencies that is no higher than the statutory FCP. The FCP is based on the Non-FAMP, which we calculate and report to the VA on a quarterly and annual basis. We also participate in the Tricare program, under which we pay quarterly rebates on utilization of innovator products that are dispensed through the Tricare Retail Pharmacy network to Tricare beneficiaries. The rebates are calculated as the difference between the annual Non-FAMP and FCP. Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts, which can change and evolve over time.

In addition, in the U.S., drug pricing by pharmaceutical companies is currently, and is expected to continue to be, under close scrutiny, including with respect to companies that have increased the price of products after acquiring those products from other companies. There are numerous ongoing efforts at the federal and state level seeking to indirectly or directly regulate drug prices to reduce overall healthcare costs using tools such as price ceilings, value-based pricing and increased transparency and disclosure obligations. Numerous states have passed or are considering legislation that requires or purports to require companies to report pricing information, including proprietary pricing information. For example, in 2017, California adopted a prescription drug price transparency state bill requiring advance notice of and an explanation for price increases of certain drugs that exceed a specified threshold. Additionally, some individual states have begun establishing Prescription Drug Affordability Boards to review high-cost drugs and, in some cases, set upper payment limits. Similar bills have been previously introduced at the federal level and additional legislation could be introduced in the near future.

Similar to what is occurring in the U.S., political, economic and regulatory developments outside of the U.S. are also subjecting the healthcare industry to fundamental changes and challenges. Pressure by governments and other stakeholders on prices and reimbursement levels continue to exist. In various EU member states, we expect to be subject to continuous cost-cutting measures, such as voluntary and temporary sales rebates, lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative. HTA of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including countries representing major markets. The HTA process, which is governed by the national laws of these countries, is the procedure according to which the assessment of the public health impact, therapeutic impact and the economic and societal impact of use of a given medicinal product in the national healthcare systems of the individual country is conducted. HTA generally compares attributes of individual medicinal products, as compared with other treatment options available on the market. The outcome of HTA regarding specific medicinal products will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. In December 2021, the EC adopted a HTA regulation intended to boost cooperation among EU member states in assessing health technologies, including new medicinal products. The HTA regulation entered into application in January 2025 and provides that EU member states must use common HTA tools, methodologies, and procedures across the EU. However, individual EU member states continue to be responsible for drawing conclusions on the overall value of a new health technology for their healthcare system, and pricing and reimbursement decisions.

In the EU, our products are marketed through various channels and within different legal frameworks. The making available or placing on the EU market of unauthorized medicinal products is generally prohibited. However, the competent authorities of the EU member states may exceptionally and temporarily allow and reimburse the supply of such unauthorized products, either on a named patient basis or through a compassionate use process, to individual patients or a group of patients with a chronically or seriously debilitating disease or whose disease is considered to be life-threatening, and who cannot be treated satisfactorily by an authorized medicinal product. Such reimbursement may no longer be available if authorization for named patient or compassionate use programs expire or is terminated or if marketing authorization is granted for the product. In some EU member states, authorization and reimbursement policies may also delay commercialization of our products, or may adversely affect our ability to sell our products on a profitable basis. After initial price and reimbursement approvals, reductions in prices and changes in reimbursement levels can be triggered by multiple factors, including reference pricing systems and publication of discounts by third party payors or authorities in other countries. In the EU, prices can be reduced further by parallel distribution and parallel trade, or arbitrage between low-priced and high-priced EU member states.

For more information, including with respect to recent legal developments regarding the Medicaid Drug Rebate Program, Medicare Part B, and the 340B program, see the risk factors under the headings “*Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and group purchasing organizations, which could diminish our sales or affect our ability to sell our products profitably; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement that could diminish our sales,*” “*The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition*” and “*If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects*” in Part I, Item 1A of this Annual Report on Form 10-K.

Patient Copay Assistance and Free Product Programs

We have various patient programs to help patients access and pay for our products, including co-pay coupons for certain products, services that help patients determine their insurance coverage for our products, and a free product program. We also make grants to independent charitable foundations that help financially needy patients with their premium, and co-pay and co-insurance obligations. There has been enhanced scrutiny of company-sponsored patient assistance programs, including co-pay assistance programs and donations to third-party charities that provide such assistance, as well as reimbursement support offerings.

The OIG has established guidelines for pharmaceutical manufacturers who make donations to charitable organizations providing co-pay assistance to Medicare patients. Such donations are unlikely to run afoul of the anti-kickback laws provided that the organizations receiving donations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. In 2016 and 2017, we received subpoenas from the U.S. Attorney's Office for the District of Massachusetts requesting documents related to our support of charitable organizations that provide financial assistance to Medicare patients. In April 2019, we finalized our civil settlement agreement with the DOJ and OIG, and entered into a corporate integrity agreement requiring us to maintain our ongoing corporate compliance program and obligating us to

implement or continue, as applicable, a set of defined corporate integrity activities to ensure compliance with OIG's policies around charitable contributions for a period of five years from the effective date of the corporate integrity agreement. As of August 2024, we have fulfilled the terms and OIG closed out our corporate integrity agreement.

About Jazz Pharmaceuticals plc

Jazz Pharmaceuticals plc was formed under the laws of Ireland (registered number 399192) as a private limited liability company in March 2005 under the name Azur Pharma Limited and was subsequently re-registered as a public limited company under the name Azur Pharma Public Limited Company in October 2011. On January 18, 2012, the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma were combined in a merger transaction, in connection with which Azur Pharma was re-named Jazz Pharmaceuticals plc and we became the parent company of and successor to Jazz Pharmaceuticals, Inc.

Our predecessor, Jazz Pharmaceuticals, Inc., was incorporated in California in March 2003 and was reincorporated in Delaware in January 2004.

Available Information

The mailing address of our headquarters is Fifth Floor, Waterloo Exchange, Waterloo Road, Dublin 4, Ireland, and our telephone number at that location is 353-1-634-7800. Our website is www.jazzpharmaceuticals.com.

We file or furnish pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, as applicable, our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, amendments to those reports, proxy statements and other information electronically with the SEC. Through a link on our website, we make copies of our periodic and current reports, amendments to those reports, proxy statements and other information available, free of charge, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

Item 1A. Risk Factors

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. The risks described below are not the only ones we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Our business could be harmed by any of these risks. The trading price of our ordinary shares could decline due to any of these risks, and you may lose all or part of your investment. In assessing these risks, you should also refer to the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and accompanying notes.

Risks Related to Our Lead Products and Product Candidates

Our inability to maintain revenues from our oxybate franchise would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Historically, our business was substantially dependent on Xyrem, and our financial results were significantly influenced by sales of Xyrem. Our current operating plan assumes that Xywav, with 92% lower sodium compared to high-sodium oxybates (depending on the dose) and absence of a sodium warning, will remain the #1 branded oxybate treatment for narcolepsy; the position it held based on revenue in the fourth quarter of 2024. While we expect that our business will continue to be meaningfully dependent on oxybate revenues, there is no guarantee that oxybate revenues will remain at current levels. In this regard, our ability to maintain oxybate revenues and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties as discussed in greater detail below, including: those related to the commercialization of Xywav for the treatment of IH in adults and adoption in that indication; competition from the introduction of AG versions of high-sodium oxybate and branded products, such as Avadel's once-nightly dose, high-sodium oxybate branded product Lumryz, for treatment of cataplexy and/or EDS in adults with narcolepsy in the U.S. market, as well as potential future competition from additional AG and generic versions of high-sodium oxybate and from other competitors; increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including our ability to maintain adequate coverage and reimbursement for Xywav and Xyrem; increased rebates required to maintain access to our products; challenges to our intellectual property around Xyrem and/or Xywav, including from pending antitrust and intellectual property litigation; and continued acceptance of Xywav and Xyrem by physicians and patients. In addition, a wholly owned subsidiary of Hikma launched its AG version of high-sodium oxybate in January 2023 and Amneal launched its AG version of high-sodium oxybate in July 2023. For a discussion of risks associated with maintaining the AG royalty revenue from these AG products, see the risk factor below titled "*The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products.*" We have seen a negative impact and expect to see a further negative impact on our oxybate revenues as a result of these AG products and Avadel's Lumryz and any generic products and new branded products. A substantial decline in oxybate revenues could cause us to reduce our operating expenses or seek to raise additional

funds and would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including on our ability to acquire, in-license or develop new products to grow our business.

The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products.

New treatment options for cataplexy and EDS in narcolepsy have been commercially launched and, in the future, other products may be launched that are competitive with or disrupt the market for our oxybate products, Xywav and Xyrem.

Ten companies have sent us notices that they had filed ANDAs seeking approval to market a generic version of Xyrem. We filed patent lawsuits against all ten companies and have settled with all ten of the companies. To date, FDA has approved or tentatively approved four of these ANDAs, and we believe that it is likely that FDA will approve or tentatively approve some or all of the others. Pursuant to our patent litigation settlement with the first filer, Hikma launched its AG version of high-sodium oxybate in the U.S. beginning on January 1, 2023. Accordingly, beginning in January 2023, Xywav and Xyrem face competition from an AG version of high-sodium oxybate. We also granted Hikma a license to launch its own generic high-sodium oxybate product but, if it elects to launch its own generic product, Hikma will no longer have the right to sell the Hikma AG product. In our settlements with Amneal, Lupin, and Par, we granted each party the right to sell a limited volume of an AG product in the U.S. beginning on July 1, 2023 and ending on December 31, 2025, with royalties to be paid to us. Amneal launched its AG version of high-sodium oxybate in July 2023. At this time, Amneal has rights to sell a low-single-digit percentage of historical Xyrem sales over each 6-month sales period. At this time, Lupin and Par have elected not to launch an AG product. AG products are distributed through the same REMS as Xywav and Xyrem. We also granted each of Amneal, Lupin and Par a license to launch its own generic high-sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including the circumstance where Hikma elects to launch its own generic product. If Amneal, Lupin or Par elects to launch its own generic product under such circumstance, it will no longer have the right to sell an AG product. In our settlements with each of six other ANDA filers, we granted each a license to launch its own generic high-sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including circumstances where Hikma launches its own generic high-sodium oxybate product. It is possible that additional companies may file ANDAs seeking to market a generic version of Xyrem which could lead to additional patent litigation or challenges with respect to Xyrem and/or additional competition for our oxybate products.

Any ANDA holder launching an AG product or another generic high-sodium oxybate product will independently establish the price of the AG product and/or its own generic high-sodium oxybate product and determine the types of discounts or rebates they will offer parties that purchase or pay for the product. Generic competition often results in decreases in the net prices at which branded products can be sold. A component of drug pricing is the manufacturer's list price for a drug to wholesalers or direct purchasers in the U.S. (without discounts, rebates or other reductions) referred to as the WAC. In this regard, Hikma and Amneal launched their AG products in 2023 at a WAC that was less than 15% lower than the WAC for Xyrem. After any introduction of a generic product, whether or not it is an AG product, a significant percentage of the prescriptions written for Xyrem have been, and will likely continue to be, filled with the generic product. Certain U.S. state laws allow for, and in some instances in the absence of specific instructions from the prescribing physician mandate, the dispensing of generic products rather than branded products when a generic version is available. This has resulted in reduced sales of, and revenue from, Xyrem. We continue to receive royalties and other revenue based on sales of AG products in accordance with the terms of our settlement agreements.

Other companies may develop sodium oxybate products for the treatment of narcolepsy, using an alternative formulation or a different delivery technology, and seek approval in the U.S. using an NDA approval pathway under Section 505(b)(2) and referencing the safety and efficacy data for Xyrem. For example, we face competition from branded products for treatment of cataplexy and/or EDS in narcolepsy, such as Avadel's Lumryz. On May 1, 2023, Avadel announced that it had received FDA approval and ODE through May 1, 2030 for Lumryz, a fixed-dose, high-sodium oxybate which uses its proprietary technology for the treatment of EDS and cataplexy in patients with narcolepsy. For additional information on litigation involving this matter, see "FDA Litigation" in Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Xyrem and Xywav also face increased competition from other branded entrants to treat EDS in narcolepsy such as pitolisant and Sunosi. Other companies have announced that they have product candidates in various phases of development to treat the symptoms of narcolepsy, such as Axsome's reboxetine, and various companies are performing research and development on orexin agonists for the treatment of sleep disorders.

We expect that Xywav for the treatment of both cataplexy and EDS in patients with narcolepsy will continue to face competition from generic or AG high-sodium oxybate products or branded entrants in narcolepsy, such as Avadel's Lumryz, notwithstanding FDA recognizing ODE for Xywav. For example, we received notices in June 2021 and February 2023, that Lupin and Teva, respectively, filed ANDAs for generic versions of Xywav. On October 13, 2023, Lupin announced that it has received tentative approval for its application to market a generic version of Xywav. We have filed patent infringement suits against these ANDA filers. For additional information see "Xywav Patent Litigation" in Note 13, Commitments and

Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Additional companies may file ANDAs seeking to market a generic version of Xywav which could lead to additional patent litigation or challenges with respect to Xywav and/or additional competition.

Moreover, generic or AG high-sodium oxybate products or branded high-sodium oxybate entrants in narcolepsy, such as Avadel's Lumryz, as well as non-oxybate products intended for the treatment of EDS or cataplexy in narcolepsy or IH including new market entrants, even if not directly competitive with Xywav or Xyrem, have had and may continue to have the effect of changing treatment regimens and payor or formulary coverage of Xywav or Xyrem in favor of other products, and indirectly adversely affect sales of Xywav and Xyrem. Examples of such new market entrants of non-oxybate products include pitolisant, a drug that was approved by FDA in 2019 for the treatment of EDS in adult patients with narcolepsy and approved by FDA in 2020 for an adult cataplexy indication in the U.S. Pitolisant has also been approved and marketed in Europe to treat adult patients with narcolepsy, with or without cataplexy, and to treat EDS in obstructive sleep apnea. Harmony Biosciences has announced a phase 3 study for pitolisant for IH after receiving a refusal to file from FDA in February 2025. In addition, we are also aware that prescribers often prescribe branded or generic medications for cataplexy and IH, before or instead of prescribing oxybate therapy including Xywav and Xyrem, and that payors often require patients to try such medications before they will cover Xywav or Xyrem, even if they are not approved for this use. Examples of such products are described in "Business—Competition" in Part I, Item 1 of this Annual Report on Form 10-K.

We expect that the approval and launch of AG products or other generic versions of Xyrem or Xywav and the approval and launch of any other sodium oxybate product, such as Avadel's Lumryz, or alternative product that treats narcolepsy will continue to have a negative impact on, and could have a material adverse effect on, our sales of Xywav and Xyrem and on our business, financial condition, results of operations and growth prospects.

The distribution and sale of our oxybate products are subject to significant regulatory restrictions, including the requirements of a REMS and safety reporting requirements, and these regulatory and safety requirements subject us to risks and uncertainties, any of which could negatively impact sales of Xywav and Xyrem.

The API of Xywav and Xyrem is a form of GHB, a central nervous system depressant known to be associated with facilitating sexual assault as well as with respiratory depression and other serious side effects. As a result, FDA requires that we maintain a REMS with ETASU for Xywav and Xyrem to help ensure that the benefits of the drug in the treatment of cataplexy and EDS in narcolepsy outweigh the serious risks of the drug. The REMS imposes extensive controls and restrictions on the sales and marketing of Xywav and Xyrem that we are responsible for implementing. Any failure to demonstrate our substantial compliance with our REMS obligations, or a determination by FDA that the REMS is not meeting its goals, could result in enforcement action by FDA, lead to changes in our REMS obligations, negatively affect sales of Xywav or Xyrem, result in additional costs and expenses for us and/or require us to invest a significant amount of resources, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

FDA continues to evaluate the Xywav and Xyrem REMS on an ongoing basis and has required, and may in the future require, modifications to the Xywav and Xyrem REMS. In 2023, FDA requested certain modifications to the Xywav and Xyrem REMS, which FDA approved in January 2024 as part of additional modifications to the REMS that we requested. We cannot predict whether FDA will request, seek to require or ultimately require additional modifications to, or impose additional requirements on, the Xywav and Xyrem REMS, including in connection with the submission of new oxybate products or indications, the introduction of AGs, or to accommodate generics, or whether FDA will approve modifications to the Xywav and Xyrem REMS that we consider warranted. Any modifications approved, required or rejected by FDA could change the safety profile of Xywav or Xyrem, and have a significant negative impact in terms of product liability, public acceptance of Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy or Xywav as a treatment for IH, and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our business. Modifications approved, required or rejected by FDA could also make it more difficult or expensive for us to distribute Xywav or Xyrem, make distribution easier for oxybate competitors, disrupt continuity of care for Xywav or Xyrem patients and/or negatively affect sales of Xywav or Xyrem.

We depend on outside vendors, including ESSDS, the central certified pharmacy, to distribute Xywav and Xyrem in the U.S., provide patient support services and implement the requirements of the Xywav and Xyrem REMS. If the central pharmacy fails to meet the requirements of the Xywav and Xyrem REMS applicable to the central pharmacy or otherwise does not fulfill its contractual obligations to us, moves to terminate our agreement, refuses or fails to adequately serve patients, or fails to promptly and adequately address operational challenges or challenges in implementing REMS modifications, the fulfillment of Xywav or Xyrem prescriptions and our sales would be adversely affected. If we change to a new central pharmacy, new contracts might be required with government payors and other insurers who pay for Xywav or Xyrem, and the terms of any new contracts could be less favorable to us than current agreements. In addition, any new central pharmacy would need to be registered with the DEA, and certified under the REMS and would also need to implement the particular processes, procedures and activities necessary to distribute under the Xywav and Xyrem REMS. Transitioning to a new pharmacy could result in product shortages, which would negatively affect sales of Xywav and Xyrem, result in additional costs and expenses

for us and/or take a significant amount of time, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

In its approval of Hikma's ANDA, FDA waived the requirement of a single shared REMS with the Xywav and Xyrem REMS, approving Hikma's ANDA with a generic high-sodium oxybate REMS separate from the Xywav and Xyrem REMS, except for the requirement that the high-sodium oxybate REMS program pharmacies contact the Xywav and Xyrem REMS by phone to verify and report certain information. The generic high-sodium oxybate REMS was approved with the condition that it be open to all future sponsors of ANDAs or NDAs for high-sodium oxybate products. In its approval of Avadel's high-sodium oxybate product, FDA also approved a separate REMS for that product, also with a requirement that the pharmacies in the Avadel-sponsored REMS contact the Xywav and Xyrem REMS to verify and report certain information. Administration of multiple sodium oxybate REMS systems could increase the risks associated with oxybate distribution, could make it more difficult or expensive for us to distribute Xywav and Xyrem and disrupt patient access to Xywav or Xyrem. Because patients, consumers and others may not differentiate other high-sodium oxybate products from our sodium oxybate products or differentiate between the different REMS programs, any negative outcomes, including risks to the public, caused by or otherwise related to a separate high-sodium oxybate REMS, could have a significant negative impact in terms of product liability, our reputation and good will, public acceptance of Xywav or Xyrem as a treatment for cataplexy and EDS in narcolepsy or Xywav for the treatment of IH, and prescribers' willingness to prescribe, and patients' willingness to take, Xywav or Xyrem, any of which could have a material adverse effect on our business.

We may face pressure to further modify the Xywav and Xyrem REMS, including sharing data, which may be proprietary, required for the safe distribution of sodium oxybate, in connection with FDA's approval of the generic sodium oxybate REMS or another oxybate REMS that has been approved or may be submitted or approved in the future. We cannot predict the outcome or impact on our business of any future action that we may take with respect to FDA's waiver of the single shared system REMS requirement, its approval and tentative approval of generic versions of sodium oxybate or the consequences of distribution of sodium oxybate through the generic sodium oxybate REMS approved by FDA or another separate REMS.

REMS programs have increasingly drawn public scrutiny from the U.S. Congress, the FTC, the USPTO, and FDA, with allegations that such programs are used as a means of improperly blocking or delaying competition. In December 2019, as part of the Further Consolidated Appropriations Act of 2020, the U.S. Congress passed legislation known as the CREATES. CREATES is intended to prevent companies from using REMS and other restricted distribution programs as a means to deny potential competitors access to product samples that are reasonably necessary to conduct testing in support of an application that references a listed drug or biologic, and provides such potential competitors a potential private right of action if the innovator fails to timely provide samples upon request. CREATES also grants FDA additional authority regarding generic products with REMS. A further example of continued interest in REMS oversight came from the USPTO in collaboration with FDA in November 2022, when they published an RFC in the Federal Register that asked, "What policy considerations or concerns should the USPTO and FDA explore in relation to the patenting of REMS associated with certain FDA-approved products?" The comments for this RFC closed on February 6, 2023.

It is possible that the FTC, FDA or other governmental authorities could claim that, or launch an investigation into whether, we are using our REMS programs in an anticompetitive manner or have engaged in other anticompetitive practices, whether under CREATES or otherwise. The Federal Food, Drug and Cosmetic Act further states that a REMS ETASU shall not be used by an NDA holder to block or delay generic drugs or drugs covered by an application under Section 505(b)(2) from entering the market. In its 2015 letter approving the Xyrem REMS, FDA expressed concern that we were aware that the Xyrem REMS is blocking competition. From June 2020 to May 2022, we were served with a number of lawsuits that included allegations that we had used the Xyrem REMS to delay approval of generic high-sodium oxybate. In December 2020, these cases were centralized and transferred to the United States District Court for the Northern District of California, where the multidistrict litigation will proceed for the purpose of discovery and pre-trial proceedings. For additional information on these lawsuits, see "*Xyrem Antitrust Litigation*" (and for other litigation involving our listing of our REMS patent in FDA's publication "Approved Drug Products with Therapeutic Equivalence Evaluations," or Orange Book, see "*Avadel Litigation*") in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations or that governmental authorities could commence an investigation. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Pharmaceutical companies, including their agents and employees, are required to monitor adverse events occurring during the use of their products and report them to FDA. The patient counseling and monitoring requirements of the Xywav and Xyrem REMS provide more extensive information about adverse events experienced by patients taking Xywav and Xyrem, including deaths, than is generally available for other products that are not subject to similar REMS requirements. As required by FDA and other regulatory agencies, the adverse event information that we collect for Xywav and Xyrem is regularly

reported to FDA and could result in FDA requiring changes to Xywav and/or Xyrem labeling, including additional warnings or additional boxed warnings, or requiring us to take other actions that could have an adverse effect on patient and prescriber acceptance of Xywav and Xyrem. As required by FDA, Xywav's and Xyrem's current labeling includes a boxed warning regarding the risk of central nervous system depression and misuse and abuse.

Any failure to demonstrate our substantial compliance with the REMS or any other applicable regulatory requirements to the satisfaction of FDA or another regulatory authority could result in such regulatory authorities taking actions in the future which could have a material adverse effect on oxybate product sales and therefore on our business, financial condition, results of operations and growth prospects.

Our inability to maintain or increase sales of Epidiolex/Epidyolex would have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our ability to maintain or increase sales of Epidiolex/Epidyolex (cannabidiol) is subject to many risks. There are many factors that could cause the commercialization of Epidiolex to be unsuccessful, including a number of factors that are outside our control. The commercial success of Epidiolex depends on the extent to which patients and physicians accept and adopt Epidiolex as a treatment for seizures associated with LGS, DS and TSC, and we do not know whether our or others' estimates in this regard will be accurate. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex. In the future, we expect Epidiolex to face competition from generic cannabinoids. In November and December 2022, we received notices from various ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex (cannabidiol) oral solution. In January 2023, we filed patent infringement suits against these ANDA filers. For additional information see "*Epidiolex Patent Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Additional companies may file ANDAs seeking to market a generic version of Epidiolex which could lead to additional patent litigation or challenges with respect to Epidiolex.

While we expect Xywav and Epidiolex/Epidyolex to remain our largest products, our success also depends on our ability to effectively commercialize our other existing products and potential future products.

In addition to Xywav, Epidiolex/Epidyolex and our other neuroscience products and product candidates, we are commercializing a portfolio of products, including our other lead marketed products, Zepzelca, Rylaze and Ziihera. An inability to effectively commercialize our other lead marketed products and to maximize their potential where possible through successful research and development activities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Our ability to realize the anticipated benefits from our investment in Zepzelca is subject to a number of risks and uncertainties, including: our ability to successfully commercialize Zepzelca in the U.S. and Canada; adequate supply of Zepzelca to meet demand; availability of favorable treatment pathway designations pricing and adequate coverage and reimbursement; the potential for negative trial data read-outs in ongoing or future Zepzelca clinical trials; our and PharmaMar's, ability to maintain accelerated approval or successfully complete a confirmatory study of Zepzelca; competition from a newly approved product for the treatment of extensive-stage metastatic SCLC; and patients' access to lung cancer screening, diagnosis and treatment. In July and August 2024, we received notices from Zepzelca ANDA filers. On September 11, 2024, we and PharmaMar filed a patent infringement suit against the Zepzelca ANDA Filers in the United States District Court for the District of New Jersey. For additional information see "*Zepzelca Patent Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Additional companies may file ANDAs seeking to market a generic version of Zepzelca which could lead to additional patent litigation or challenges with respect to Zepzelca.

Our ability to realize the anticipated benefits from our investments in Rylaze is subject to a number of uncertainties, including our ability to successfully commercialize Rylaze including creating awareness among health care professionals and ensuring that patients with ALL or LBL will be given the appropriate course of therapy and dosing regimen based on the currently approved label. Our ability to realize the anticipated benefits from our investments in Ziihera is subject to a number of uncertainties, including our ability to successfully commercialize Ziihera in BTC and clinical development of potential future indications in HER2+ solid tumors.

We face substantial competition from other companies, including companies with larger sales organizations and more experience working with large and diverse product portfolios, and competition from generic drugs.

Our products compete, and our product candidates may in the future compete, with currently existing therapies, including other branded products, AG and other generic products, product candidates currently under development by us and others and/or future product candidates, including new molecular and chemical entities that may be safer or more effective or more

convenient than our products. Any products that we develop may be commercialized in competitive markets, and our competitors, which include large global pharmaceutical companies and small research-based companies and institutions, may succeed in developing products that render our products obsolete or noncompetitive. Many of our competitors, particularly large pharmaceutical and life sciences companies, have substantially greater financial, operational and human resources than we do. Smaller or earlier stage companies may also prove to be significant competitors, particularly through focused development programs and collaborative arrangements with large, established companies. In addition, many of our competitors deploy more personnel to market and sell their products than we do, and we compete with other companies to recruit, hire, train and retain pharmaceutical sales and marketing personnel. If our sales force and sales support organization are not appropriately resourced and sized to adequately promote our products, the commercial potential of our current and any future products may be diminished. In any event, the commercial potential of our current products and any future products may be reduced or eliminated if our competitors develop or acquire and commercialize generic or branded products that are safer or more effective, are more convenient or are less expensive than our products. If we are unable to compete successfully, our commercial opportunities will be reduced and our business, results of operations and financial conditions may be materially harmed.

For a description of the competition that our lead marketed products and most advanced product candidates face or may face, see the discussion in “Business—Competition” in Part I, Item 1 of this Annual Report on Form 10-K and the risk factor under the heading “*The introduction of new products in the U.S. market that compete with, or otherwise disrupt the market for, our oxybate products has adversely affected and may continue to adversely affect sales of our oxybate products*” in this Part I, Item 1A.

Recent executive and judicial changes and flux in the regulatory landscape creates uncertainty for us and our industry.

The current administration is pursuing policies to reduce regulations and expenditures across government including at HHS, FDA, CMS and related agencies. These actions, presently directed by executive orders or memoranda from the Office of Management and Budget, may propose policy changes that create additional uncertainty for our business. These actions may include directives to reduce agency workforce, rescinding a Biden administration executive order tasking the Center for Medicare & Medicaid Innovation to consider new payment and healthcare models to limit drug spending and eliminating the Biden administration’s executive order that directed HHS to establish an AI task force and develop a strategic plan. Additionally, in its June 2024 decision in *Loper Bright*, the U.S. Supreme Court overturned the longstanding *Chevron* doctrine, under which courts were required to give deference to regulatory agencies’ reasonable interpretations of ambiguous federal statutes. The *Loper Bright* decision could result in additional legal challenges to current regulations and guidance issued by federal agencies applicable to our operations, including those issued by FDA. Finally, Congress may introduce and ultimately pass health care related legislation that could impact the drug approval process and make changes to the Medicare Drug Price Negotiation Program created under the IRA. We cannot predict which additional measures may be adopted or the impact of current and additional measures on the marketing, pricing and demand for our products, which could have a material adverse effect on our business, financial condition and results of operations.

Adequate coverage and reimbursement from third party payors may not be available for our products and we may be unable to successfully contract for coverage from pharmacy benefit managers and other organizations; conversely, to secure coverage from these organizations, we may be required to pay rebates or other discounts or other restrictions to reimbursement, either of which could diminish our sales or adversely affect our ability to sell our products profitably.

In both U.S. and non-U.S. markets, our ability to successfully commercialize and achieve market acceptance of our products depends in significant part on adequate financial coverage and reimbursement from third party payors, including governmental payors (such as the Medicare and Medicaid programs in the U.S.), managed care organizations and private health insurers. Without third party payor reimbursement, patients may not be able to obtain or afford prescribed medications. In addition, reimbursement guidelines and incentives provided to prescribing physicians by third party payors may have a significant impact on the prescribing physicians’ willingness and ability to prescribe our products. The demand for, and the profitability of, our products could be materially harmed if state Medicaid programs, the Medicare program, other healthcare programs in the U.S. or elsewhere, or third party commercial payors in the U.S. or elsewhere, deny reimbursement for our products, limit the indications for which our products will be reimbursed, or provide reimbursement only on unfavorable terms.

As part of the overall trend toward cost containment, third party payors often require prior authorization for, and require reauthorization for continuation of, prescription products or impose step edits, which require prior use of another medication, usually a generic or preferred brand, prior to approving coverage for a new or more expensive product. Such restrictive conditions for reimbursement and an increase in reimbursement-related activities can extend the time required to fill prescriptions and may discourage patients from seeking treatment. We cannot predict actions that third party payors may take, or whether they will limit the access and level of reimbursement for our products or refuse to provide any approvals or coverage. From time to time, third party payors have refused to provide reimbursement for our products, and others may do so in the future.

Third party payors increasingly examine the cost-effectiveness of pharmaceutical products, in addition to their safety and efficacy, when making coverage and reimbursement decisions. We may need to conduct expensive pharmacoeconomic and/or clinical studies in order to demonstrate the cost-effectiveness of our products. If our competitors offer their products at prices that provide purportedly lower treatment costs than our products, or otherwise suggest that their products are safer, more effective or more cost-effective than our products, this may result in a greater level of access for their products relative to our products, which would reduce our sales and harm our results of operations. In some cases, for example, third party payors try to encourage the use of less expensive generic products through their prescription benefit coverage and reimbursement and co-pay policies. Because some of our products compete in a market with both branded and generic products, obtaining and maintaining access and reimbursement coverage for our products may be more challenging than for products that are new chemical entities for which no therapeutic alternatives exist.

Third party PBMs, other similar organizations and payors can limit coverage to specific products on an approved list, or formulary, which might: not include all of the approved products for a particular indication, exclude drugs from their formularies in favor of competitor drugs or alternative treatments, place drugs on formulary tiers with higher patient co-pay obligations, and/or mandate stricter utilization criteria. Formulary exclusion effectively encourages patients and providers to seek alternative treatments, make a complex and time-intensive request for medical exemptions, or pay 100% of the cost of a drug. In addition, in many instances, certain PBMs, other similar organizations and third party payors may exert negotiating leverage by requiring incremental rebates, discounts or other concessions from manufacturers in order to maintain formulary positions, which could continue to result in higher gross to net deductions for affected products. The market for PBM services has become highly concentrated and vertically integrated, giving these entities further leverage in negotiating rebates, discounts or other concessions. In this regard, we have entered into agreements with PBMs and payor accounts to provide rebates to those entities related to formulary coverage for our products, but we cannot guarantee that we will be able to agree to coverage terms with other PBMs and other third party payors. Payors could decide to exclude our products from formulary coverage lists, impose step edits that require patients to try alternative, including generic, treatments before authorizing payment for our products, limit the types of diagnoses for which coverage will be provided or impose a moratorium on coverage for products while the payor makes a coverage decision. An inability to maintain adequate formulary positions could increase patient cost-sharing for our products and cause some patients to determine not to use our products. Any delays or unforeseen difficulties in reimbursement approvals could limit patient access, depress therapy adherence rates, and adversely impact our ability to successfully commercialize our products. In addition, PBMs and other third-party payors could implement alternative funding programs that could have an impact on product revenue. If we are unsuccessful in maintaining broad coverage for our products, our anticipated revenue from and growth prospects for our products could be negatively affected.

In many countries outside the U.S., procedures to obtain price approvals, coverage and reimbursement can take considerable time after the receipt of marketing authorization. Many European countries periodically review their reimbursement of medicinal products, which could have an adverse impact on reimbursement status. In addition, we expect that legislators, policymakers and healthcare insurance funds in the EU member states will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU member states, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. HTA of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU member states, including those representing the larger markets. The HTA process, which is currently governed by national laws in each EU member state, is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU member states. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU member states. In January 2025, the EU HTA regulation entered into application. This regulation aims to harmonize the clinical benefit assessment of HTA across the EU. Under this regulation, EU member states must use common HTA tools, methodologies, and procedures across the EU. However, individual member states remain responsible for determining the overall value of a new health technology within their healthcare systems, as well as making pricing and reimbursement decisions. If we are unable to maintain favorable pricing and reimbursement status in EU member states that represent significant markets, our anticipated revenue from and growth prospects for our products in the EU could be negatively affected. For example, the EC granted marketing authorization for Enrylaze in September 2023, and, as part of our rolling launch of Enrylaze in Europe, we are making pricing and reimbursement submissions in European countries. If we experience setbacks or unforeseen difficulties in obtaining favorable pricing and reimbursement decisions, including as a result of regulatory review delays, planned launches in the affected EU member states would be delayed, which could negatively impact anticipated revenue from and growth prospects for Enrylaze.

The pricing of pharmaceutical products has come under increasing scrutiny as part of a global trend toward healthcare cost containment and resulting changes in healthcare law and policy, including changes to Medicare, may impact our business in ways that we cannot currently predict, which could have a material adverse effect on our business and financial condition.

Political, economic and regulatory influences are subjecting the healthcare industry in the U.S. to fundamental changes, particularly given the current atmosphere of mounting criticism of prescription drug costs in the U.S. We expect there will continue to be legislative and regulatory proposals to change the healthcare system in ways that could impact our ability to sell our products profitably, as governmental oversight and scrutiny of biopharmaceutical companies is increasing. For example, we anticipate that the U.S. Congress, state legislatures, and federal and state regulators may adopt or accelerate adoption of new healthcare policies and reforms intended to curb healthcare costs, such as federal and state controls on reimbursement for drugs (including under Medicare, Medicaid and commercial health plans), new or increased requirements to pay prescription drug rebates and penalties to government health care programs, and additional pharmaceutical cost transparency policies that aim to require drug companies to justify their prices through required disclosures. This includes efforts by individual states in the U.S. to pass legislation and implement regulations designed to control pharmaceutical and biological product pricing, including by establishing Prescription Drug Affordability Boards (or similar entities) to review high-cost drugs and, in some cases, set upper payment limits and implementing marketing cost disclosure and transparency measures. Further, the IRA, among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs and a change in manufacturer liability under the program, which could negatively affect our business and financial condition. The CMS has issued final guidance implementing the Drug Price Negotiation Program in which it finalized certain policies governing the selection of drugs for negotiation. Among other things, CMS finalized definitions of “qualifying single source drug” and “marketed” that, especially if they persist, could further disincentivize innovation. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are no longer subject to a cap on the rebate amount effective January 1, 2024, which may adversely affect our rebate liability.

Legislative and regulatory proposals that have recently been considered include, among other things, proposals to limit the terms of patent litigation settlements with generic sponsors, to define certain conduct around patenting and new product development as unfair competition, to address the scope of orphan drug exclusivity and to facilitate the importation of drugs into the U.S. from other countries. Legislative and regulatory proposals to reform the regulation of the pharmaceutical industry and reimbursement for pharmaceutical drugs are continually changing, and all such considerations may adversely affect our business and industry in ways that we cannot accurately predict.

There is also ongoing activity related to health care coverage. The Affordable Care Act substantially changed the way healthcare is financed by both governmental and private insurers. These changes impacted previously existing government healthcare programs and have resulted in the development of new programs, including Medicare payment-for-performance initiatives. Further, federal and state policy makers have taken and may continue to try to take steps regarding health care coverage beyond the Affordable Care Act, which could have ramifications for the pharmaceutical industry. Additional legislative changes, regulatory changes, or guidance could be adopted, which may impact the marketing approvals and reimbursement for our products and product candidates. For example, there has been increasing legislative, regulatory, and enforcement interest in the U.S. with respect to drug pricing practices. There have been several Congressional inquiries and proposed and enacted federal and state legislation and regulatory initiatives designed to, among other things, bring more transparency to product pricing, evaluate the relationship between pricing and manufacturer patient programs, and reform government healthcare program reimbursement methodologies for drug products beyond the changes enacted by the IRA.

If new healthcare policies or reforms intended to curb healthcare costs are adopted or if we experience negative publicity with respect to pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for our products may be affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. We have periodically increased the price of our products, including Xywav and Xyrem most recently in January 2025, and there is no guarantee that we will make similar price adjustments to our products in the future or that price adjustments we have taken or may take in the future will not negatively affect our sales volumes and revenues. There is no guarantee that such price adjustments will not negatively affect our reputation and our ability to secure and maintain reimbursement coverage for our products, which could limit the prices that we charge for our products, limit the commercial opportunities for our products and/or negatively impact revenues from sales of our products.

Government investigations or U.S. Congressional oversight with respect to drug pricing or our other business practices could cause us to incur significant expense and could distract us from the operation of our business and execution of our strategy. Any such investigation or hearing could also result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our

business, financial condition, results of operations and growth prospects. For more information, see the risk factor under the heading “*We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products*” in Part I, Item 1A of this Annual Report on Form 10-K.

We expect that legislators, policymakers and healthcare insurance funds in Europe and other international markets will continue to propose and implement cost-containing measures to keep healthcare costs down. These measures could include limitations on the prices we will be able to charge for our products or the level of reimbursement available for these products from governmental authorities or third party payors as well as clawbacks and revenue caps. For example, in the U.K., the cap on NHS spending on branded medicines agreed between the U.K. government and industry for 2019 to 2023 has remained unaltered despite higher than expected growth in NHS use of branded medicines, resulting in significant increases to the industry level revenue clawback rate payable on sales of branded medicines to the NHS. In the EU, a trend in some EU member states is for medicinal products to be reimbursed based on competitor products and not in relation with the value or the cost of the product. On April 26, 2023, the EC adopted proposals for a new Directive and a new Regulation, which revise and replace the existing EU general pharmaceutical legislation. This proposal includes increased transparency on research and development costs or public contributions to these costs with a view to strengthen the negotiating position of national competent authorities of the EU member states responsible for pricing and reimbursement, as well as reinforced cooperation with these authorities on pricing and reimbursement matters. On April 10, 2024, the European Parliament adopted its position on the proposals, whose legislative processes are expected to continue in 2025. Further, an increasing number of European and other foreign countries use prices for medicinal products established in other countries as “reference prices” to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

In addition to access, coverage and reimbursement, the commercial success of our products depends upon their market acceptance by physicians, patients, third party payors and the medical community.

If physicians do not prescribe our products, we cannot generate the revenues we anticipate from product sales. Market acceptance of each of our products by physicians, patients, third party payors and the medical community depends on:

- the clinical indications for which a product is approved and any restrictions placed upon the product in connection with its approval, such as a REMS or equivalent obligation imposed in a European or other foreign country, patient registry requirements or labeling restrictions;
- the prevalence of the disease or condition for which the product is approved and its diagnosis;
- the efficacy of the product in regular use;
- the severity of side effects and other risks in relation to the benefits of our products;
- unanticipated serious adverse events;
- acceptance by physicians and patients of each product as a safe and effective treatment;
- availability of sufficient product inventory to meet demand;
- physicians’ decisions relating to treatment practices based on availability of product;
- perceived clinical superiority and/or advantages over alternative treatments;
- overcoming negative publicity surrounding illicit use of
 - GHB or
 - CBD and marijuana products

and the view of patients, law enforcement agencies, physicians and regulators of our products as being the same or similar to illicit products;

- relative convenience and ease of administration;
- with respect to Xywav and Xyrem, physician and patient assessment of the burdens associated with obtaining or maintaining the certifications required under the Xywav and Xyrem REMS;
- the cost of treatment in relation to alternative treatments, including generic products; and
- the availability of financial or other assistance for patients who are uninsured or underinsured.

Because of our dependence upon market acceptance of our products, any adverse publicity associated with harm to patients or other adverse events resulting from the use or misuse of any of our products or any similar products distributed by

other companies, including generic versions of our products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Delays or problems in the supply of our products for sale or for use in clinical trials, loss of our single source suppliers or failure to comply with manufacturing regulations could materially and adversely affect our business, financial condition, results of operations and growth prospects.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the API and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. We and our suppliers may encounter difficulties in production, including difficulties with the supply of manufacturing materials, production costs and yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state and non-U.S. regulations. In addition, we and our suppliers are subject to FDA's cGMP requirements, federal and state controlled substances obligations and equivalent rules and regulations prescribed by non-U.S. regulatory authorities. If we or any of our suppliers encounter manufacturing, quality or compliance difficulties with respect to any of our products, whether due to the ongoing military conflict in Ukraine and related sanctions imposed against Russia (including as a result of disruptions of global shipping, the transport of products, energy supply, cybersecurity incidents and banking systems as well as of our ability to control input costs) or otherwise, we may be unable to obtain or maintain regulatory approval or meet commercial demand for such products, which could adversely affect our business, financial condition, results of operations and growth prospects. In addition, we could be subject to enforcement action by regulatory authorities for our failure to comply with cGMP with respect to the products we manufacture in our facilities as well as for our failure to adequately oversee compliance with cGMP by any of our third party suppliers operating under contract. Moreover, failure to comply with applicable legal and regulatory requirements subjects us and our suppliers to possible regulatory action, including restrictions on supply or shutdown, which may adversely affect our or a supplier's ability to supply the ingredients or finished products we need.

We have a manufacturing and development facility in Athlone, Ireland where we manufacture Xywav and Xyrem, a manufacturing plant in Villa Guardia, Italy where we produce the defibrotide drug substance and a manufacturing and development facility in the U.K. at Kent Science Park, where we produce Epidiolex/Epidyolex and have capability to develop product candidates. We currently do not have our own commercial manufacturing or packaging capability for our other products, their APIs or product candidates outside of those developed at Kent Science Park. As a result, our ability to develop and supply products in a timely and competitive manner depends primarily on third party suppliers being able to meet our ongoing commercial and clinical trial needs for API, other raw materials, packaging materials and finished products.

In part due to the limited market size for our products and product candidates, we have a single source of supply for most of our marketed products, product candidates and their APIs. Single sourcing puts us at risk of interruption in supply in the event of manufacturing, quality or compliance difficulties. If one of our suppliers fails or refuses to supply us for any reason, it would take a significant amount of time and expense to implement and execute the necessary technology transfer to, and to qualify, a new supplier. FDA and similar international or national regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in our products. If there are delays in qualifying new suppliers or facilities or a new supplier is unable to meet FDA's or similar international regulatory body's requirements for approval, there could be a shortage of the affected products for the marketplace or for use in clinical studies, or both, which could negatively impact our anticipated revenues and could potentially cause us to breach contractual obligations with customers or to violate local laws requiring us to deliver the product to those in need.

We are responsible for the manufacture and supply of Epidiolex/Epidyolex for commercial use and for use in clinical trials. The manufacturing of Epidiolex/Epidyolex necessitates compliance with GMP, and other regulatory requirements in jurisdictions internationally. Our ability to successfully manufacture Epidiolex/Epidyolex involves cultivation of botanical raw material from specific cannabinoid plants, extraction and purification processes, manufacture of finished products and labeling and packaging, which includes product information, tamper evidence and anti-counterfeit features, under tightly controlled processes and procedures. In addition, we must ensure chemical consistency among our batches, including clinical batches and, if approved, marketing batches. Demonstrating such consistency may require typical manufacturing controls as well as clinical data. We must also ensure that our batches conform to complex release specifications. We have a second site at which we can grow the specific cannabinoid plants that produce the CBD used in Epidiolex/Epidyolex and a second site at which we can crystallize the purified CBD from the liquid plant extract. If we are unable to manufacture Epidiolex/Epidyolex in accordance with regulatory specifications, including GMP, or if there are disruptions in our manufacturing process due to damage, loss or otherwise, or failure to pass regulatory inspections of our manufacturing facilities, we may not be able to meet current demand or supply sufficient product for use in clinical trials, and this may also harm our ability to commercialize Epidiolex/Epidyolex on a timely or cost-competitive basis, if at all. Our manufacturing program requires significant time and resources and may not be successful, may lead to delays, interruptions to supply or may prove to be more costly than anticipated.

Vyxeos is manufactured by Simtra, which is a sole source supplier from a single site location. Moreover, the proprietary technology that supports the manufacture of Vyxeos is not easily transferable. Consequently, engaging an alternate manufacturer may be difficult, costly and time-consuming. If we fail to obtain a sufficient supply of Vyxeos in accordance with applicable specifications on a timely basis, our sales of Vyxeos, our future maintenance and potential growth of the market for this product, our ability to conduct ongoing and future clinical trials of Vyxeos, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

Rylaze drug substance is manufactured by AGC Biologics A/S at its facility in Copenhagen, Denmark and the drug product is manufactured and packaged by Patheon at its facility in Greenville, North Carolina. To successfully manufacture Rylaze, the manufacturer must have an adequate master and working cell bank. If we fail to obtain a sufficient supply of Rylaze in accordance with applicable specifications on a timely basis, our sales of Rylaze, our future maintenance and potential growth of the market for this product, our competitive advantage over competing products that have supply constraints, and our business, financial condition, results of operations and growth prospects could be materially adversely affected.

We currently rely on WuXi, a company based in the PRC, as the sole supplier of Ziihera. Accordingly, there is a risk that supplies of Ziihera may be significantly delayed by, or may become unavailable as a result of, manufacturing, equipment, process, regulatory or business-related issues affecting that company. We may also face additional manufacturing and supply-chain risks due to the regulatory and political structure of the PRC, or as a result of the international relationship between the PRC and the U.S., including but not limited to potential trade restrictions, sanctions, other regulatory requirements, or proposed legislation imposed by the U.S. government, which could restrict or even prohibit our ability to work with WuXi. For example, the House of Representatives of the prior Congress (the 118th Congress) passed the BIOSECURE Act, which proposed targeting U.S. government contracts, grants and loans for entities that use biotechnology equipment or services from certain named Chinese biotechnology companies, including WuXi, and potentially other biotechnology companies designated in the future. The language of the proposed BIOSECURE Act would, among other things, prohibit U.S. federal agencies from entering into or renewing any contract with any entity that uses biotechnology equipment or services produced or provided by a "biotechnology company of concern." The version of the bill passed by the prior House of Representatives included a "grandfathering" provision, which provided that the BIOSECURE Act's prohibitions would not apply to pre-existing contracts and agreements entered into prior to the legislation's effective date until 2032. The BIOSECURE Act did not become law in the 118th Congress. It is unclear whether the current Congress (the 119th Congress) will introduce the BIOSECURE Act or similar legislation in this congressional session and, if so, how the scope, prohibitions, or designated biotechnology companies of concern may differ from the version of the BIOSECURE Act passed by the House in the prior 118th Congress. Although to date there has been no impact on our ability to obtain supply of Ziihera, there can be no assurance that operations would not be impacted in the future with a negative impact on Ziihera supply.

In addition, in order to conduct our ongoing and any future clinical trials of, complete marketing authorization submissions for, and potentially launch our other product candidates, we also need to have sufficient quantities of product manufactured. Moreover, to obtain approval from FDA or a similar international or national regulatory body of any product candidate we or our suppliers for that product must obtain approval by the applicable regulatory body to manufacture and supply product, in some cases based on qualification data provided to the applicable body as part of our regulatory submission. Any delay in generating, or failure to generate, data required in connection with submission of the chemistry, manufacturing and controls portions of any regulatory submission could negatively impact our ability to meet our anticipated submission dates, and therefore our anticipated timing for obtaining FDA or similar international or national regulatory body approval, or our ability to obtain regulatory approval at all. In addition, any failure of us or a supplier to obtain approval by the applicable regulatory body to manufacture and supply product or any delay in receiving, or failure to receive, adequate supplies of a product on a timely basis or in accordance with applicable specifications could negatively impact our ability to successfully launch and commercialize products and generate sales of products at the levels we expect.

Global trade issues and changes in and uncertainties with respect to trade policies and export regulations, including import and export license requirements, trade sanctions, tariffs and international trade disputes, could adversely impact our business and operations, and reduce the competitiveness of our products and services relative to local and global competitors.

There is inherent risk, based on the complex relationships among the U.S. and the countries in which we conduct our business, that political, diplomatic, and national security factors can lead to global trade restrictions and changes in trade policies and export regulations that may adversely affect our business and operations. Compliance with applicable regulatory requirements regarding the export of our products may create delays in the introduction of our products in international markets or, in some cases, prevent the export of our products to some countries altogether. Furthermore, U.S. export control laws and economic sanctions prohibit the provision of certain products and services to countries, governments and persons targeted by U.S. sanctions. The U.S. and other countries have imposed and may continue to impose new trade restrictions and export regulations, have levied tariffs and taxes on certain goods, and could significantly increase tariffs on a broad array of goods. For example, on February 1, 2025, President Donald Trump signed executive orders imposing a 25% tariff on certain imports

from Mexico and Canada, and a 10% tariff on certain imports from China, which were to take effect on February 4, 2025. A 30-day pause was granted to Mexico and Canada. However, these newly proposed and imposed tariffs have resulted in retaliatory tariffs, and threats thereof, against U.S. goods. The ultimate impact of these potential and actual tariffs on our business and financial condition is unknown. In addition, ongoing changes in U.S. and foreign government trade policies, including potential modifications to existing trade agreements, could introduce additional uncertainty. Trade restrictions and export regulations, or increases in tariffs (including tariffs on imports from Europe) and additional taxes, including any retaliatory measures, can negatively impact end-user demand, increase our supply chain complexity and our manufacturing costs, decrease margins, reduce the competitiveness of our products, or restrict our ability to sell products, provide services or purchase necessary equipment and supplies, any or all of which could have a material and adverse effect on our business, results of operations, or financial condition and, given the nature of our products, relocating the manufacturing supply can be a complex, costly and time-consuming process making it difficult to react quickly to a changing environment.

Risks Related to Growth of Our Product Portfolio and Research and Development

Our future success depends on our ability to successfully obtain and maintain regulatory approvals for our late-stage product candidates and, if approved, to successfully launch and commercialize those product candidates.

The testing, manufacturing and marketing of our products require regulatory approvals, including approval from FDA and similar bodies in Europe and other countries. If FDA, EMA, the EC or the competent authorities of the EU member states or other European countries determine that our quality, safety or efficacy data do not warrant marketing approval for a product candidate, we could be required to conduct additional clinical trials as a condition to receiving approval, which could be costly and time-consuming and could delay or preclude the approval of our application. Our inability to obtain and maintain regulatory approval for our product candidates in the U.S. and internationally and to successfully commercialize new products that are approved would prevent us from receiving a return on our investments and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Even if we receive regulatory approval of a product, regulatory authorities may impose significant labeling restrictions or requirements, including limitations on the dosing of the product, requirements around the naming or strength of a product, restrictions on indicated uses for which we may market the product, the imposition of a boxed warning or other warnings and precautions, and/or the requirement for a REMS or equivalent obligation imposed in a European or other foreign country to ensure that the benefits of the drug outweigh the risks. FDA requires a REMS and a boxed warning for Xywav and Xyrem, and similar restrictions could be imposed on other products in the future. Our receipt of approval for narrower indications than sought, restrictions on marketing through a REMS or equivalent obligation imposed in a European or other foreign country, or significant labeling restrictions or requirements in an approved label such as a boxed warning, could have a negative impact on our ability to recoup our research and development costs and to successfully commercialize that product, any of which could materially and adversely affect our business, financial condition, results of operations and growth prospects.

Regulatory authorities may also impose post-marketing obligations as part of their approval, which may lead to additional costs and burdens associated with commercialization of the product and may pose a risk to maintaining approval of the product. We are subject to certain post-marketing requirements and commitments in connection with the approval of certain of our products, including Epidiolex/Epidyolex, Defitelio, Vyxeos, Rylaze, Zepzelca and Ziihera. These post-marketing requirements and commitments include satisfactorily conducting multiple post-marketing trials and safety studies. Failure to comply with these post-marketing requirements could result in withdrawal of our marketing approvals for the applicable product and/or other civil or criminal penalties. If a product is approved under accelerated approval, continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial. For example, FDA granted accelerated approval to Zepzelca for relapsed SCLC based on data from a Phase 2 trial, which approval is contingent upon verification and description of clinical benefit in a post-marketing clinical trial. While we and our licensor PharmaMar have reached agreement with FDA regarding a confirmatory clinical development program, our inability to confirm its clinical benefit in the second-line treatment setting for SCLC could result in the withdrawal of approval of Zepzelca, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In addition, FDA granted accelerated approval to Ziihera for previously treated, unresectable or metastatic HER2-positive BTC based on data from a Phase 2 trial. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. While a Phase 3 confirmatory trial is ongoing to evaluate zanidatamab in combination with standard-of-care therapy versus standard-of-care therapy alone in the first-line setting for patients with HER2-positive BTC, our inability to confirm its clinical benefit in the first-line setting for patients with HER2-positive BTC could result in the withdrawal of approval of Ziihera, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects. In any event, if we are unable to comply with our post-marketing obligations imposed as part of the marketing approvals in the U.S., the EU, or other countries, our approval may be varied, suspended or revoked, product supply may be delayed and our sales of our products could be materially adversely affected.

Any new data relating to Epidiolex/Epidyolex, including from adverse event reports and post-marketing studies in the U.S. and Europe, and from other ongoing clinical trials, may result in changes to the product label and/or imposition of a REMS

and may adversely affect sales, or result in withdrawal of Epidiolex/Epidyolex from the market. FDA, EMA and regulatory authorities in other jurisdictions may also consider the new data in reviewing Epidiolex/Epidyolex marketing applications for indications beyond its currently approved uses or impose additional post-approval requirements. If any of these actions were to occur, it could result in significant expense and delay or limit our ability to generate sales of Epidiolex/Epidyolex.

If we are not successful in the clinical development of our product candidates, if we are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, in each case including as a result of any executive or judicial actions as described under “—Recent executive and judicial changes and flux in the regulatory landscape creates uncertainty for us and our industry,” our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We may not be able to successfully identify and acquire or in-license additional products or product candidates to grow our business, and, even if we are able to do so, we may otherwise fail to realize the anticipated benefits of these transactions.

In addition to continued investment in our research and development pipeline, we intend to grow our business by acquiring or in-licensing, and developing, including with collaboration partners, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. However, we may be unable to identify or consummate suitable acquisition or in-licensing opportunities, and this inability could impair our ability to grow our business. Other companies, many of which may have substantially greater financial, sales and marketing resources, compete with us for these opportunities. Even if appropriate opportunities are available, we may not be able to successfully identify them, or we may not have the financial resources necessary to pursue them.

Even if we are able to successfully identify and acquire, in-license or develop additional products or product candidates, we may not be able to successfully manage the risks associated with integrating any products or product candidates into our portfolio or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing or from financial difficulties of our collaborators. Further, while we seek to mitigate risks and liabilities of potential acquisitions and in-licensing transactions through, among other things, due diligence, there may be risks and liabilities that such due diligence efforts fail to discover, that are not disclosed to us, or that we inadequately assess. Any failure in identifying and managing these risks, liabilities and uncertainties effectively, could have a material adverse effect on our business, results of operations and financial condition. In addition, product and product candidate acquisitions, particularly when the acquisition takes the form of a merger or other business consolidation, such as our acquisition of GW have required, and any similar future transactions also will require, significant efforts and expenditures, including with respect to transition and integration activities. We may encounter unexpected difficulties, or incur substantial costs, in connection with potential acquisitions and similar transactions, which include:

- the need to incur substantial debt and/or engage in dilutive issuances of equity securities to pay for acquisitions;
- the need to comply with regulatory requirements, including in some cases clearance from the FTC;
- the potential need to secure shareholder approval of the transaction;
- the potential disruption of our historical core business;
- the strain on, and need to continue to expand, our existing operational, technical, financial and administrative infrastructure;
- the difficulties in integrating acquired products and product candidates into our portfolio;
- the difficulties in assimilating employees and corporate cultures;
- the failure to retain key managers and other personnel;
- the need to write down assets or recognize impairment charges;
- the diversion of our management’s attention to integration of operations and corporate and administrative infrastructures; and
- any unanticipated liabilities for activities of or related to the acquired business or its operations, products or product candidates.

As a result of these or other factors, products or product candidates we acquire, or obtain licenses to, may not produce the revenues, earnings or business synergies that we anticipated, may not result in regulatory approvals, and may not perform as expected. For example, in May 2021, we made a substantial investment in Epidiolex and certain other products and technologies acquired in our acquisition of GW. The total consideration paid by us for the entire issued share capital of GW was \$7.2 billion. The success of our acquisition of GW will depend, in part, on our ability to realize the anticipated benefits from the acquisition, which benefits may not be realized at the expected levels within the expected timeframe, or at all, or may

take longer to realize or cost more than expected, which could materially and adversely affect our business, financial condition, results of operations and growth prospects. In this regard, in the third quarter of 2022, we recorded a \$133.6 million asset impairment charge as a result of the decision to discontinue the nabiximols program that we acquired as part of our acquisition of GW. In any event, failure to manage effectively our growth through acquisitions or in-licensing transactions could adversely affect our growth prospects, business, results of operations and financial condition.

Conducting clinical trials is costly and time-consuming, and the outcomes are uncertain. A failure to prove that our product candidates are safe and effective in clinical trials, or to generate data in clinical trials to support expansion of the therapeutic uses for our existing products, could materially and adversely affect our business, financial condition, results of operations and growth prospects.

As a condition to regulatory approval, each product candidate must undergo extensive and expensive preclinical studies and clinical trials to demonstrate that the product candidate is safe and effective. The results at any stage of the development process may lack the desired safety, efficacy or pharmacokinetic characteristics. If FDA or any equivalent non-U.S. regulatory agency determines that the safety or efficacy data included in any marketing application we submit do not warrant marketing approval for the affected product or product candidate, we may be required to conduct additional preclinical studies or clinical trials, which could be challenging to perform, costly and time-consuming. Even if we believe we have successfully completed testing, FDA or any equivalent non-U.S. regulatory agency may determine our data is not sufficiently compelling to warrant marketing approval for the indication(s) sought, if at all, and may require us to engage in additional clinical trials or provide further analysis which may be costly and time-consuming. Any adverse events or other data generated during the course of clinical trials of our product candidates and/or clinical trials related to additional indications for our commercialized products could result in action by FDA, or an equivalent non-U.S. regulatory agency, which may restrict our ability to sell, or adversely affect sales of, currently marketed products, or such events or other data could otherwise have a material adverse effect on a related commercial product, including with respect to its safety profile. Any failure or delay in completing such clinical trials could materially and adversely affect the maintenance and growth of the markets for the related marketed products, which could adversely affect our business, financial condition, results of operations and overall growth prospects.

In addition to issues relating to the results generated in clinical trials, clinical trials have been and can be delayed or halted for a variety of reasons, including:

- difficulty identifying, recruiting or enrolling eligible patients, often based on the number of clinical trials, particularly with enrollment criteria targeting the same patient population, and in rare diseases with small patient populations;
- difficulty identifying a clinical development pathway, including viable indications and appropriate clinical trial protocol design, particularly where there is no applicable regulatory precedent;
- delays or failures in obtaining regulatory authorization to commence a trial because of safety concerns of regulators relating to our product candidates or similar product candidates of our competitors or failure to follow regulatory guidelines;
- delays or failures in obtaining clinical materials and manufacturing sufficient quantities of the product candidate for use in trials;
- delays or failures in reaching agreement on acceptable terms with prospective study sites;
- delays or failures in obtaining approval of our clinical trial protocol from an institutional review board, or similar bodies in other jurisdictions, such as an ethics committee in Europe, to conduct a clinical trial at a prospective study site;
- failure of our clinical trials and clinical investigators, including contract research organizations or other third parties assisting us with clinical trials, to satisfactorily perform their contractual duties, meet expected deadlines and comply with FDA and other regulatory agencies' requirements, including good clinical practices;
- unforeseen safety issues;
- inability to monitor patients adequately during or after treatment;
- difficulty monitoring multiple study sites; or
- insufficient funds to complete the trials.

In some jurisdictions such as the EU, initiating Phase 3 clinical trials and clinical trials in the pediatric population is subject to a requirement to obtain approval or a waiver from the competent authorities of the EU member states and/or EMA. If we do not obtain such approval, our ability to conduct clinical trials and obtain marketing authorizations or approvals may be severely impaired and our business may be adversely impacted.

Risks Related to Our Intellectual Property

It is difficult and costly to protect our proprietary rights, and we may not be able to ensure their protection.

Our commercial success depends in part on obtaining, maintaining and defending intellectual property protection for our products and product candidates, including protection of their use and methods of manufacturing. Our ability to protect our products and product candidates from unauthorized making, using, selling, offering to sell or importation by third parties depends on the extent to which we have rights under valid and enforceable patents or have adequately protected trade secrets that cover these activities.

The degree of protection to be afforded by our proprietary rights is difficult to predict because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- our patent applications, or those of our licensors or partners, may not result in issued patents;
- others may independently develop similar or therapeutically equivalent products without infringing our patents, or those of our licensors, such as products that are not covered by the claims of our patents, or for which fall outside the exclusive rights granted under our license agreements;
- our issued patents, or those of our licensors or partners, may be held invalid or unenforceable as a result of legal challenges by third parties or may be vulnerable to legal challenges as a result of changes in applicable law;
- our patents covering certain aspects of our products or the use thereof could be delisted from FDA's Orange Book as a result of challenges by third parties before FDA or the courts;
- competitors may manufacture products in countries where we have not applied for patent protection or that have a different scope of patent protection or that do not respect our patents; or
- others may be issued patents that prevent the sale of our products or require licensing and the payment of significant fees or royalties.

Patent enforcement generally must be sought on a country-by-country basis, and patent validity and infringement may be judged differently in different countries. The legal systems of certain countries, particularly certain developing countries, may lack maturity or consistency when it comes to the enforcement of patents and other intellectual property rights, particularly those relating to pharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business.

Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property portfolio. Any patent may be challenged, and potentially invalidated or held unenforceable, including through patent litigation or through administrative procedures that permit challenges to patent validity. Patents can also be designed around by an ANDA or Section 505(b)(2) NDA that avoids infringement of our intellectual property.

In June 2021, we received notice from Lupin that it has filed with FDA an ANDA for a generic version of Xywav. The notice from Lupin included a "paragraph IV certification" with respect to ten of our patents listed in FDA's Orange Book for Xywav on the date of our receipt of the notice. A paragraph IV certification is a certification by a generic applicant that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product. In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. In February 2023, we received notice from Teva that it had filed an ANDA seeking approval to market a generic version of Xywav, which notice included a paragraph IV certification with respect to certain of our patents listed in FDA's Orange Book for Xywav. For additional information on litigation involving these matters, see Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

We have settled patent litigation with each of the ten companies seeking to introduce generic versions of Xyrem in the U.S. by granting those companies licenses to launch their generic products (and in certain cases, an AG version of Xyrem) in advance of the expiration of the last of our patents. Notwithstanding our Xyrem patents and settlement agreements, additional third parties may also attempt to introduce generic versions of Xyrem, Xywav or other sodium oxybate products for treatment of cataplexy and/or EDS in narcolepsy that design around our patents or assert that our patents are invalid or otherwise unenforceable. Such third parties could launch a generic or 505(b)(2) product referencing Xyrem before the dates provided in our patents or settlement agreements. For example, we have several methods of use patents listed in the Orange Book, that expire in 2033 that cover treatment methods included in the Xyrem label related to a DDI with divalproex sodium. Although FDA has stated, in granting a Citizen Petition we submitted in 2016, that it would not approve any sodium oxybate ANDA referencing Xyrem that does not include the portions of the currently approved Xyrem label related to the DDI patents, we

cannot predict whether a future ANDA filer, or a company that files a Section 505(b)(2) application for a drug referencing Xyrem, may pursue regulatory strategies to avoid infringing our DDI patents notwithstanding FDA's response to the Citizen Petition, or whether any such strategy would be successful. Likewise, we cannot predict whether we will be able to maintain the validity of these patents or will otherwise obtain a judicial determination that a generic or other sodium oxybate product, its package insert or the generic sodium oxybate REMS or another separate REMS will infringe any of our patents or, if we prevail in proving infringement, whether a court will grant an injunction that prevents a future ANDA filer or other company introducing a different sodium oxybate product from marketing its product, or instead require that party to pay damages in the form of lost profits or a reasonable royalty.

Since Xyrem's regulatory exclusivity has expired in the EU, we are aware that generic or hybrid generic applications have been approved by various EU regulatory authorities, and additional generic or hybrid generic applications may be submitted and approved.

Additionally, in November and December 2022, ten companies sent us notices that they had filed ANDAs seeking approval to market a generic version of Epidiolex, which notices each included a paragraph IV certification with respect to certain of our patents listed in FDA's Orange Book for Epidiolex on the date of the receipt of the applicable notice. On January 3, 2023, we filed a patent infringement suit against the ten Epidiolex ANDA filers in the United States District Court for the District of New Jersey. In June and July 2023, we received notice from certain of the Epidiolex ANDA Filers that they had each filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Epidiolex. On July 21, 2023, we filed an additional lawsuit against all of the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey alleging that, by filing its ANDA, each Epidiolex ANDA Filer infringed the newly-issued patent related to a method of treatment using Epidiolex. For additional information on litigation involving this matter, see "*Epidiolex Patent Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

On May 13, 2021, we filed a patent infringement suit against Avadel and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's product candidate FT218 will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. In March 2024, the jury upheld the validity of both of our asserted patents and awarded us damages for infringement for past sales of Lumryz in the U.S. For additional information on litigation involving this matter, see "*Avadel Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

In July and August 2024, Zepzelca ANDA filers sent us notices that they had filed ANDAs seeking approval to market a generic version of Zepzelca (lurbinectedin), which notices each included a paragraph IV certification with respect to our Orange Book listed patent for Zepzelca on the date of the receipt of the applicable notice. In September 2024, we filed patent infringement suits against these ANDA filers. For additional information on litigation involving this matter, see "*Zepzelca Patent Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

We also currently rely in part on trade secret protection for several of our products, including Defitelio, and product candidates. Trade secret protection does not protect information or inventions if another party develops that information or invention independently and establishing that a competitor developed a product through trade secret misappropriation rather than through legitimate means may be difficult to prove. We seek to protect our trade secrets and other unpatented proprietary information in part through confidentiality and invention agreements with our employees, consultants, advisors and partners. Nevertheless, our employees, consultants, advisors and partners may unintentionally or willfully disclose our proprietary information to competitors, and we may not have adequate remedies for such disclosures. Moreover, if a dispute arises with our employees, consultants, advisors or partners over the ownership of rights to inventions, including jointly developed intellectual property, we could lose patent protection or the confidentiality of our proprietary information, and possibly also lose the ability to pursue the development of certain new products or product candidates.

We have incurred, and may in the future incur, substantial costs as a result of litigation or other proceedings relating to patents, other intellectual property rights and related matters, and we may be unable to protect our rights to, or commercialize, our products.

Our ability, and that of our partners, to successfully commercialize any approved products will depend, in part, on our ability to obtain patents, enforce those patents and operate without infringing the proprietary rights of third parties. If we choose to go to court to stop a third party from infringing our patents, our licensed patents or our partners' patents, that third party has the right to ask the court or an administrative agency to rule that these patents are invalid and/or should not be enforced. These lawsuits and administrative proceedings are expensive and consume time and other resources, and we may not be successful in these proceedings or in stopping infringement. In addition, the IPR or a post-grant review process under the

Leahy-Smith America Invents Act permits any person, whether they are accused of infringing the patent at issue or not, to challenge the validity of certain patents through a proceeding before the PTAB of the USPTO.

There is a risk that a court could decide that our patents or certain claims in our patents are not valid or infringed, and that we do not have the right to stop a third party from using the inventions covered by those claims. In addition, the PTAB may invalidate a patent, as happened with six of our patents covering the Xywav and Xyrem REMS that were invalidated through the IPR process. In addition, even if we prevail in establishing that another product infringes a valid claim of one of our patents, a court may determine that we can be compensated for the infringement in damages, and refuse to issue an injunction. As a result, we may not be entitled to stop another party from infringing our patents for their full term.

Litigation involving patent matters is frequently settled between the parties, rather than continuing to a court ruling. The FTC has publicly stated that, in its view, certain types of agreements between branded and generic pharmaceutical companies related to the settlement of patent litigation or the manufacture, marketing and sale of generic versions of branded drugs violate the antitrust laws and has commenced investigations and brought actions against some companies that have entered into such agreements. In particular, the FTC has expressed its intention to take aggressive action to challenge settlements that include an alleged transfer of value from the brand company to the generic company (so-called “pay for delay” patent litigation settlements). The U.S. Congress and state legislatures have also identified pharmaceutical patent litigation settlements as potential impediments to generic competition and have introduced, and in states like California passed, legislation to regulate them. Third party payors have also challenged such settlements on the grounds that they increase drug prices. Because there is currently no precise legal standard with respect to the lawfulness of such settlements, many pharmaceutical companies, including us, have faced extensive litigation over whether patent litigation settlements they have entered into are reasonable and lawful. From June 2020 to May 2022, several lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with Hikma and other ANDA filers violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits, see “*Xyrem Antitrust Litigation*” in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs in the class action complaints were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Parties to such settlement agreements in the U.S. are required by law to file the agreements with the FTC and the DOJ for review. Accordingly, we have submitted our patent litigation settlement agreements to the FTC and the DOJ for review. We may receive formal or informal requests from the FTC regarding our ANDA litigation settlements, and there is a risk that the FTC may commence a formal investigation or action against us, which could divert the attention of management and cause us to incur significant costs, regardless of the outcome. Any claim or finding that we or our business partners have failed to comply with applicable laws and regulations could be costly to us and have a material adverse effect on our business, financial condition, results of operations and growth prospects.

A third party may claim that we or our manufacturing or commercialization partners are using inventions covered by the third party’s patent rights, or that we or such partners are infringing, misappropriating or otherwise violating other intellectual property rights, and may go to court to stop us from engaging in our normal operations and activities, including making or selling our products. Such lawsuits are costly and could affect our results of operations and divert the attention of management and development personnel. There is a risk that a court could decide that we or our partners are infringing, misappropriating or otherwise violating third party patent or other intellectual property rights, which could be very costly to us and have a material adverse effect on our business. If we are sued for patent infringement, we would need to demonstrate that our products or methods do not infringe the patent claims of the relevant patent and/or that the patent claims are invalid or unenforceable, which we may not be able to do.

If we were found to infringe upon a patent or other intellectual property right, if we failed to obtain or renew a license under a patent or other intellectual property right from a third party, or if a third party that we were licensing technologies from was found to infringe upon a patent or other intellectual property rights of another third party, we may be required to pay damages, including damages of up to three times the damages found or assessed, if the infringement is found to be willful, suspend the manufacture of certain products or reengineer or rebrand our products, if feasible, or we may be unable to enter certain new product markets. In addition, if we have declined or failed to enter into a valid assignment agreement for any reason, we may not own the invention or our intellectual property, and our products may not be adequately protected.

Litigation, whether filed by us or against us, can be expensive and time consuming to defend and divert management’s attention and resources. Our competitive position could suffer as a result. On June 22, 2023, we filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA’s approval on May 1, 2023 of the NDA for Avadel’s drug Lumryz was unlawful. On September 15, 2023, we filed a motion for summary judgment. On October 20, 2023, Avadel and FDA filed cross motions for summary judgment. Oral argument on these motions was held on May 10, 2024, and

On October 30, 2024, the District Court issued an order denying our motion for summary judgment and granting Avadel's and FDA's cross-motions for summary judgment. We have appealed the matter to the United States Court of Appeals for the District of Columbia Circuit. We cannot predict the timing or ultimate outcome of this litigation or the impact of this litigation on our business, including any potential adverse consequences to, among other things, our reputation, relationships with governmental or regulatory authorities, including FDA. For additional information, see "*FDA Litigation*" in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

With respect to our products and product candidates targeting rare indications, relevant regulatory exclusivities such as orphan drug exclusivity or pediatric exclusivity may not be granted or, if granted, may be limited.

The first NDA applicant with an orphan drug designation for a particular active moiety to treat a specific disease or condition that receives FDA approval is usually entitled to a seven-year exclusive marketing period in the U.S. for that drug, for that indication. We rely in part on this ODE and other regulatory exclusivities to protect Xywav, Epidiolex, Zepzelca, Ziihera and, potentially, our other products and product candidates from competitors, and we expect to continue relying in part on these regulatory exclusivities in the future. The duration of our regulatory exclusivity period could be impacted by a number of factors, including FDA's later determination that our request for orphan designation was materially defective, that the manufacturer is unable to supply sufficient quantities of the drug, that the extension of the exclusivity period established by the Improving Regulatory Transparency for New Medical Therapies Act does not apply, or the possibility that we are unable to successfully obtain pediatric exclusivity. There is no assurance that we will successfully obtain orphan drug designation for other products or product candidates or other rare diseases or that a product candidate for which we receive orphan drug designation will be approved, or that we will be awarded ODE upon approval as, for example, FDA may reconsider whether the eligibility criteria for such exclusivity have been met and/or maintained. Moreover, a drug product with an active moiety that is different from that in our drug candidate or, under limited circumstances, the same drug product, may be approved by FDA for the same indication during the period of marketing exclusivity. According to FDA, the limited circumstances include a showing that the second drug is clinically superior to the drug with marketing exclusivity through a demonstration of superior safety or efficacy or that it makes a major contribution to patient care. For example, even though FDA granted seven-year ODE to Xywav, FDA also approved Lumryz and granted Lumryz seven-year ODE based on FDA's finding that Lumryz makes a major contribution to patient care and is therefore clinically superior to Xywav and Xyrem. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for the same indication before us, approval of our product candidate would be blocked during the period of marketing exclusivity unless we could demonstrate that our product candidate is clinically superior to the approved product. In addition, if a competitor obtains approval and marketing exclusivity for a drug product with an active moiety that is the same as that in a product candidate we are pursuing for a different orphan indication, this may negatively impact the market opportunity for our product candidate. There have been legal challenges, including from us, to aspects of FDA's regulations and policies concerning the exclusivity provisions of the Orphan Drug Act, including whether two drugs are the same drug product, and our and future challenges could lead to changes that affect the protections potentially afforded our products in ways that are difficult to predict. In this regard, we have filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA's approval of Lumryz was unlawful and allege that FDA acted outside its authority under the Orphan Drug Act, when, despite the ODE protecting Xywav, FDA approved Lumryz and granted Lumryz seven-year ODE. However, legal challenges like this are inherently uncertain and there can be no guarantee that the United States District Court for the District of Columbia will agree with our interpretation of applicable laws and regulations or will otherwise agree with any or all of the allegations included in our complaint, or that we will otherwise prevail in this litigation. We also cannot predict what other adverse consequences to, among other things, our reputation, our relationship with FDA or other governmental or regulatory authorities or the protections afforded our products could result from our decision to proceed with this litigation or the ultimate outcome thereof. Moreover, in the future, there is the potential for legislative changes or additional legal challenges to FDA's orphan drug regulations and policies, and it is uncertain how such challenges might affect our business.

In the EU, if a marketing authorization is granted for a medicinal product designated an orphan drug, that product is currently entitled to ten years of marketing exclusivity. We rely in part on this orphan drug exclusivity and other regulatory exclusivities to protect Epidyolex and Vyxeos. During the period of marketing exclusivity, subject to limited exceptions, no similar medicinal product may be granted a marketing authorization for the orphan indication. There is no assurance that we will successfully obtain orphan drug designation for future rare indications or orphan exclusivity upon approval of any of our product candidates that have already obtained designation. On April 26, 2023, the EC published proposals for a new package of pharmaceutical legislation that would replace the current Medicines Directive and the existing medicinal product regulation (including the pediatric and orphan regulations). If enacted, the proposal could impact our ability to secure orphan designation for future products, and would impact the scope and duration of market and orphan exclusivities in the EU. Further, a similar medicinal product may be granted a marketing authorization for the same indication notwithstanding our marketing exclusivity if we are unable to supply sufficient quantities of our product, or if the second product is safer, more effective or otherwise clinically superior to our orphan drug. In addition, if a competitor obtains marketing authorization and orphan exclusivity for a

product that is similar to a product candidate we are pursuing for the same indication, approval of our product candidate would be blocked during the period of orphan marketing exclusivity unless we could demonstrate that our product candidate is safer, more effective or otherwise clinically superior to the approved product.

Other Risks Related to Our Business and Industry

We have substantially expanded our international footprint and operations, and we may expand further in the future, which subjects us to a variety of risks and complexities which, if not effectively managed, could negatively affect our business.

We are headquartered in Dublin, Ireland and have offices in multiple locations, including the U.S., the U.K. and key markets across Europe, Canada, Australia and Japan and manage clinical trial sites in multiple locations around the world. We may further expand our international operations into other countries in the future, either organically or by acquisition. Conducting our business in multiple countries subjects us to a variety of risks and complexities that may materially and adversely affect our business, results of operations, financial condition and growth prospects, including:

- the diverse regulatory, financial and legal requirements in the countries where we are located or do business, and any changes to those requirements;
- challenges inherent in efficiently managing employees and commercial partners in diverse geographies, including the need to adapt systems, policies, benefits and compliance programs to differing labor and employment law and other regulations, as well as maintaining positive interactions with our unionized employees;
- costs of, and liabilities for, our international operations, including clinical trials, products or product candidates;
- additional exposure to foreign currency exchange risk from non-U.S. operations;
- political and economic instability, such as the instability caused by Russia's invasion of Ukraine;
- escalating trade tensions; and
- public health risks and potential related effects on supply chain, travel and employee health and availability.

In addition, there can be no guarantee that we will effectively manage the increasing, global complexity of our business without experiencing operating inefficiencies or control deficiencies. Our failure to do so could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Significant disruptions of information technology systems or data security breaches could adversely affect our business.

In the ordinary course of our business, we and the third parties upon which we rely collect, store, process and transmit, or collectively, process large amounts of sensitive, proprietary, and/or confidential information, including intellectual property, business information, personal data, and clinical trial data, or collectively, sensitive data. We outsource some of our operations (including parts of our information technology infrastructure) to a number of third party vendors who may have, or could gain, access to our confidential information. In addition, many of those third parties, in turn, subcontract or outsource some of their responsibilities to third parties.

Our information technology systems, and those of our vendors, are large and complex and store large amounts of sensitive data. We and the third parties upon which we rely face a variety of evolving threats that could impact the availability of our sensitive data and information technology systems and cause security incidents from inadvertent or intentional actions by our employees, third party vendors and/or business partners, or from cyber-attacks and malicious third parties.

Threats of this nature are prevalent, are increasing in frequency, persistence, sophistication and intensity, are being conducted by sophisticated and organized groups and individuals, are increasingly difficult to detect, and come from a variety of sources and with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, "hacktivists," traditional computer "hackers," threat actors, personnel (such as through theft or misuse), nation states, nation-state-supported actors, and others.

In addition to the extraction of important information, such threats could include the deployment of harmful malware, ransomware, denial-of-service attacks, social engineering, malicious code, credential harvesting, personnel misconduct or error, supply-chain attacks, software bugs, server malfunctions, software or hardware failures, loss of data or other information technology assets, adware, attacks enhanced or facilitated by AI, and other threats that affect service reliability and threaten the confidentiality, integrity and availability of our information technology systems and sensitive data. In addition, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties' infrastructure in our supply chain or our third-party partners' supply chains have not been compromised.

If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, or otherwise experience significant disruptions of our, our third party vendors' and/or business partners' information technology systems or security breaches, including in our remote work environment, such occurrence could adversely affect our

business operations and/or result in the loss, misappropriation, and/or unauthorized access, use or disclosure of, or the prevention of access to, sensitive data, and could result in adverse consequences to us such as government enforcement actions, additional reporting requirements and/or oversight, restrictions on processing sensitive data, litigation, indemnification obligations, negative publicity, reputational harm, monetary fund diversions, diversion of management attention, interruptions in our operations, financial loss, and other similar harms. Any such event that leads to unauthorized access, use or disclosure of personal data, including personal data regarding our patients or employees, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, notify relevant stakeholders, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect the privacy and security of personal data. This could disrupt our business, result in increased costs or loss of revenue, and/or result in significant legal and financial exposure. In addition, security breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may further harm us.

While we have implemented security measures to protect our information technology systems and infrastructure and sensitive data, there can be no assurance that such measures will be effective or prevent service interruptions or security breaches that could adversely affect our business. We may expend significant resources to implement and maintain security measures to try to protect against security incidents. In addition, failure to maintain effective internal accounting controls related to security breaches and cybersecurity in general could impact our ability to produce timely and accurate financial statements and subject us to regulatory scrutiny.

In addition to experiencing a security incident, third parties may gather, collect, or infer sensitive data about us from public sources, data brokers, or other means that reveals competitively sensitive details about our organization and could be used to undermine our competitive advantage or market position.

We are subject to significant ongoing regulatory obligations and oversight, which may subject us to civil or criminal proceedings, investigations, or penalties and may result in significant additional expense and limit our ability to commercialize our products.

FDA and Equivalent Non-U.S. Regulatory Authorities

Our activities are subject to extensive regulation encompassing the entire life cycle of our products, from research and development activities to marketing approval (including specific post-marketing obligations), manufacturing, labeling, packaging, adverse event and safety reporting, storage, advertising, promotion, sale, pricing and reimbursement, recordkeeping, distribution, importing and exporting. The failure by us or any of our third party partners, including our corporate development and collaboration partners, clinical trial sites, suppliers, distributors and our central pharmacy for Xywav and Xyrem, to comply with applicable requirements could subject us to administrative or judicial sanctions or other negative consequences, such as delays in approval or refusal to approve a product candidate, restrictions on our products, our suppliers, our other partners or us, the withdrawal, suspension or variation of product approval or manufacturing authorizations, untitled letters, warning letters, fines and other monetary penalties, unanticipated expenditures, product recall, withdrawal or seizure, total or partial suspension of production or distribution, interruption of manufacturing or clinical trials, operating restrictions, injunctions, suspension of licenses, civil penalties and/or criminal prosecution, any of which could result in a significant drop in our revenues from the affected products and harm to our reputation and could have a significant impact on our sales, business and financial condition.

We monitor adverse events resulting from the use of our products, as do the regulatory authorities, and we file periodic reports with the authorities concerning adverse events. The authorities review these events and reports and, if they determine that any events and/or reports indicate a trend or signal, they can require a change in a product label, restrict sales and marketing and/or require conduct or other actions, potentially including variation, withdrawal or suspension of the marketing authorization, any of which could result in reduced market acceptance and demand for our products, could harm our reputation and our ability to market our products in the future, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. FDA, the competent authorities of the EU member states on behalf of EMA, and the competent authorities of other European countries, also periodically inspect our records related to safety reporting. EMA's Pharmacovigilance Risk Assessment Committee may propose to the Committee for Medicinal Products for Human Use that the marketing authorization holder be required to take specific steps or advise that the existing marketing authorization be varied, suspended or revoked. Failure to adequately and promptly correct the observation(s) can result in further regulatory enforcement action, which could include the variation, suspension or withdrawal of marketing authorization or imposition of financial penalties or other enforcement measures.

Rylaze and Epidyolex are available on a named patient basis or through a compassionate use process in many countries where they are not commercially available. If any such country's regulatory authorities determine that we are promoting such products without proper authorization, we could be found to be in violation of pharmaceutical advertising laws or the regulations permitting sales under named patient programs. In that case, we may be subject to financial or other penalties. Any failure to maintain revenues from sales of products on a named patient basis and/or to generate revenues from commercial sales

of these products exceeding historical sales on a named patient basis could have an adverse effect on our business, financial condition, results of operations and growth prospects.

FDA, the competent authorities of the EU member states and other European countries, and other governmental authorities require advertising and promotional materials to be truthful and not misleading, and products to be marketed only for their approved indications and in accordance with the provisions of the approved label. Regulatory authorities actively investigate allegations of off-label promotion in order to enforce regulations prohibiting these types of activities. A determination that we have promoted an approved product for off-label uses could subject us to significant liability, including civil and administrative financial penalties and other remedies as well as criminal financial penalties, other sanctions and imprisonment. Even if we are not determined to have engaged in off-label promotion, an allegation that we have engaged in such activities could have a significant impact on our sales, business and financial condition. The U.S. government has also required companies to enter into complex corporate integrity agreements and/or non-prosecution agreements that impose significant reporting and other burdens on the affected companies. Failure to maintain a comprehensive and effective compliance program, and to integrate the operations of acquired businesses into a combined comprehensive and effective compliance program on a timely basis, could subject us to a range of regulatory actions and/or civil or criminal penalties that could affect our ability to commercialize our products and could harm or prevent sales of the affected products, or could substantially increase the costs and expenses of commercializing and marketing our products.

Other Regulatory Authorities

We are also subject to regulation by other regional, national, state and local agencies, including the DEA, the DOJ, the FTC, the United States Department of Commerce, the OIG, and other regulatory bodies, as well as similar governmental authorities in those non-U.S. countries in which we commercialize our products.

We are subject to numerous fraud and abuse laws and regulations globally and our sales, marketing, patient support and medical activities may be subject to scrutiny under these laws and regulations. These laws are described in “Business—Government Regulation” in Part I, Item 1 of this Annual Report on Form 10-K. While we maintain a comprehensive compliance program to try to ensure that our practices and the activities of our third party contractors and employees fall within the scope of available statutory exceptions and regulatory safe harbors whenever possible, and otherwise comply with applicable laws, regulations or guidance, regulators and enforcement agencies may disagree with our assessment or find fault with the conduct of our employees or contractors. In addition, existing regulations are subject to regulatory revision or changes in interpretation by the DOJ or OIG. For example, in November 2020, the OIG issued a Special Fraud Alert to highlight certain inherent risks of remuneration related to speaker programs sponsored by drug and medical device companies, which may not in all circumstances qualify under either safe harbor or statutory exception protection. The Special Fraud Alert sent a clear signal that speaker programs will be subject to potentially heightened enforcement scrutiny, in particular for those programs with certain characteristics identified as risk factors by OIG.

Many companies have faced government investigations or lawsuits by whistleblowers who bring a *qui tam* action under the False Claims Act on behalf of themselves and the government for a variety of alleged improper marketing activities, including providing free product to customers expecting that the customers would bill federal programs for the product, providing consulting fees, grants, free travel and other benefits to physicians to induce them to prescribe the company’s products, and inflating prices reported to private price publication services, which are used to set drug reimbursement rates under government healthcare programs. For example, we are subject to a *qui tam* whistleblower lawsuit originally filed under seal on May 27, 2021. For additional information see “*Qui tam matter*” in Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. In addition, the government and private whistleblowers have pursued False Claims Act cases against pharmaceutical companies for causing false claims to be submitted as a result of the marketing of their products for unapproved uses or violations of the federal anti-kickback statute. If we become the subject of a government False Claims Act or other investigation or whistleblower suit, we could incur substantial legal costs (including settlement costs) and business disruption responding to such investigation or suit, regardless of the outcome.

Any investigations or litigation may result in damages, fines, penalties or administrative sanctions against us, negative publicity or other negative actions that could harm our reputation, reduce demand for our products and/or reduce coverage of our products, including by federal health care programs and state health care programs. If any or all of these events occur, our business and stock price could be materially and adversely affected.

Public reporting under the Sunshine provisions, and other similar state laws, the requirements of which are discussed in “Business—Government Regulation” in Part I, Item 1 of this Annual Report on Form 10-K, has resulted in increased scrutiny of the financial relationships between industry, teaching hospitals, physicians and other health care providers. Such scrutiny may negatively impact our ability to engage with physicians and other health care providers on matters of importance to us. In addition, government agencies and private entities may inquire about our marketing practices or pursue other enforcement activities based on the disclosures in those public reports. If the data reflected in our reports are found to be in violation of any

of the Sunshine provisions or any other U.S. federal, state or local laws or regulations that may apply, or if we otherwise fail to comply with the Sunshine provisions or similar requirements of state or local regulators, we may be subject to significant civil, and administrative penalties, damages or fines.

We have various programs to help patients access our products, including patient assistance programs, which include co-pay coupons for certain of our products, assistance to help patients determine their insurance coverage for our products, and a free product program. Co-pay coupon programs for commercially insured patients, including our program for Xyrem, have received negative publicity related to allegations regarding their use to promote branded pharmaceutical products over other less costly alternatives, and some states have imposed restrictions on manufacturer co-pay programs when therapeutic equivalents are available. In September 2014, the OIG issued a Special Advisory Bulletin warning manufacturers that they may be subject to sanctions under the federal Anti-Kickback Statute and other laws if they do not take appropriate steps to exclude Medicare Part D beneficiaries from using co-pay coupons. It is possible that changes in insurer policies regarding co-pay coupons and/or the introduction and enactment of new legislation or regulatory action could restrict or otherwise negatively affect these patient support programs, which could result in fewer patients using affected products, including Xyrem, and therefore could have a material adverse effect on our sales, business and financial condition.

We have established programs to consider grant applications submitted by independent charitable organizations, including organizations that provide co-pay support to patients who suffer from the diseases treated by our drugs. The OIG has issued guidance for how pharmaceutical manufacturers can lawfully make donations to charitable organizations who provide co-pay assistance to Medicare patients, provided that such organizations, among other things, are *bona fide* charities, are entirely independent of and not controlled by the manufacturer, provide aid to applicants on a first-come basis according to consistent financial criteria, and do not link aid to use of a donor's product. As of August 2024, we have fulfilled the terms and OIG closed out our corporate integrity agreement that required us to maintain our ongoing corporate compliance program. Although we are continuing to implement our corporate compliance program and have structured our programs to follow available guidance, if we or our vendors or donation recipients are deemed to fail to comply with relevant laws, regulations or evolving government guidance in the operation of these programs, such facts could be used as the basis for an enforcement action against us by the federal government or other enforcement agencies or private litigants, or we could become liable for payment of certain stipulated penalties or could be excluded from participation in federal health care programs, which would have a material adverse effect on our sales, business and financial condition.

Our business activities outside of the U.S. are subject to the FCPA, and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the U.K. Bribery Act. In certain countries, the health care providers who prescribe pharmaceuticals are employed by their government and the purchasers of pharmaceuticals are government entities; therefore, our dealings with these prescribers and purchasers may be subject to regulation under the FCPA, the U.K. Bribery Act and equivalent national laws in other countries. Violation of these laws by us or our suppliers and other third party agents for which we may be liable may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

Outside the U.S., interactions between pharmaceutical companies and physicians are also governed by strict laws, such as national anti-bribery laws of European countries, national sunshine rules, regulations, industry self-regulation codes of conduct and physicians' codes of professional conduct. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

We are also subject to federal, state, national and international laws and regulations governing the privacy and security of health-related and other personal data we collect and maintain, including, but not limited to, Section 5 of the Federal Trade Commission Act, the Health Breach Notification Rule, HIPAA, the California Consumer Privacy Act, as amended by California Privacy Rights Act, as well as other similar state privacy laws, and the EU's and U.K.'s GDPR. The GDPR, for example, imposes restrictions on the processing (e.g., collection, use and disclosure) of personal data in the EU and the U.K. and also imposes strict restrictions on the transfer of personal data out of the EU to the U.S. The GDPR imposes penalties of up to 20 million Euros or up to 4% of annual global revenue. HIPAA imposes privacy and security obligations on covered entity health care providers, health plans, and health care clearinghouses, as well as their "business associates" – certain persons or covered entities that create, receive, maintain, or transmit protected health information in connection with providing a specified service or performing a function for or on behalf of a covered entity. Although we are not directly subject to HIPAA, we could potentially be subject to criminal penalties if we, our affiliates, or our agents knowingly receive individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA. The FTC also sets expectations for failing to take appropriate steps to keep consumers' personal information secure or failing to provide a level of security commensurate to promises made to an individual about the security of their personal information (such as in a privacy notice); such failures may constitute unfair or deceptive acts or practices in violation of Section 5(a) of the Federal Trade Commission Act. Compliance with these laws requires a flexible privacy framework and substantial resources, and compliance efforts will likely be an increasing and substantial cost in the future.

If we or our third party partners fail to comply or are alleged to have failed to comply with these or other applicable data protection and privacy laws and regulations, or if we were to experience a data breach involving personal data, we could be subject to government enforcement actions or private lawsuits. Any associated claims, inquiries, or investigations or other government actions could lead to unfavorable outcomes that have a material impact on our business including through significant penalties or fines, monetary judgments or settlements including criminal and civil liability for us and our officers and directors, increased compliance costs, delays or impediments in the development of new products, negative publicity, increased operating costs, diversion of management time and attention, or other remedies that harm our business, including orders that we modify or cease existing business practices.

If we fail to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program or other governmental pricing programs, we could be subject to additional reimbursement requirements, penalties, sanctions and fines, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

We participate in the Medicaid Drug Rebate Program, the 340B program, the U.S. Department of Veterans Affairs' FSS pricing program, and Tricare program, and have obligations to report the average sales price for certain of our drugs to the Medicare program. All of these programs are described in more detail under the heading "Business—Pharmaceutical Pricing, Reimbursement by Government and Private Payors and Patient Access" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2024. Manufacturers are required to report the average sales price for drugs under the Medicare program regardless of whether they are enrolled in the Medicaid Drug Rebate Program. In addition, manufacturers must pay refunds to Medicare for single source drugs or biologicals, or biosimilar biological products, reimbursed under Medicare Part B and packaged in single-dose containers or single-use packages for units of discarded drug reimbursed by Medicare Part B in excess of 10 percent of total allowed charges under Medicare Part B for that drug. Statutory or regulatory changes or guidance from CMS could affect the average sales price calculations for our products and the resulting Medicare payment rate and could negatively impact our results of operations. Further, the IRA established a Medicare Part B inflation rebate scheme, under which, generally speaking, manufacturers will owe rebates if the average sales price of a Part B drug increases faster than the pace of inflation. Failure to timely pay a Part B inflation rebate is subject to a civil monetary penalty.

Pricing and rebate calculations vary across products and programs, are complex, and are often subject to interpretation by us, governmental or regulatory agencies and the courts, which can change and evolve over time. In the case of our Medicaid pricing data, if we become aware that our reporting for a prior quarter was incorrect or has changed as a result of recalculation of the pricing data, we are generally obligated to resubmit the corrected data for up to three years after those data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and could result in an overage or underage in our rebate liability for past quarters. Price recalculations also may affect the ceiling price at which we are required to offer our products under the 340B program and give rise to an obligation to refund entities participating in the 340B program for overcharges during past quarters impacted by a price recalculation.

Civil monetary penalties can be applied if we are found to have knowingly submitted any false price or product information to the government, if we are found to have made a misrepresentation in the reporting of our average sales price, if we fail to submit the required price data on a timely basis, or if we are found to have charged 340B covered entities more than the statutorily mandated ceiling price. CMS could also decide to terminate our Medicaid drug rebate agreement, in which case federal payments may not be available under Medicaid or Medicare Part B for our covered outpatient drugs. We cannot be certain that our submissions will not be found by CMS to be incomplete or incorrect. Moreover, failure to pay refunds for units of discarded drug under the discarded drug refund program could subject us to civil monetary penalties of 125 percent of the refund amount.

Our failure to comply with our reporting and payment obligations under the Medicaid Drug Rebate Program and other governmental programs could negatively impact our financial results. CMS issued a final rule that modified prior Medicaid Drug Rebate Program regulations to permit reporting multiple best price figures with regard to value-based purchasing arrangements; and to provide definitions for "line extension," "new formulation," and related terms, with the practical effect of expanding the scope of drugs considered to be line extensions that are subject to an alternative rebate formula. While the regulatory modifications that purported to affect the applicability of the best price and average manufacturer price exclusions of manufacturer-sponsored patient benefit programs, in the context of PBM "accumulator" programs were invalidated by a court and rescinded, such programs may continue to negatively affect us in other ways. Our failure to comply with these price reporting and rebate payment options could negatively impact our financial results. In addition, on September 26, 2024, CMS finalized a rule modifying the regulations implementing the Medicaid Drug Rebate Program in ways that could increase the costs and complexity of compliance and that could increase manufacturer rebate liability, given that the final rule clarified certain aspects of the definition of covered outpatient drugs subject to these rebates, which could expand the number of units of drugs that qualify for this definition, among other changes. Regulatory and legislative changes, and judicial rulings relating to the Medicaid Drug Rebate Program and related policies (including coverage expansion), have increased and will continue to

increase our costs and the complexity of compliance, have been and will continue to be time-consuming to implement, and could have a material adverse effect on our results of operations, particularly if CMS or another agency challenges the approach we take in our implementation. Rebates are no longer subject to a cap on the rebate amount, which negatively impacts our rebate liability.

The HRSA issued a final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities. Implementation of this regulation could affect our obligations and potential liability under the 340B program in ways we cannot anticipate. We are also required to report the 340B ceiling prices for our covered outpatient drugs to HRSA, which then publishes them to 340B covered entities. If we are found to have knowingly and intentionally charged 340B covered entities more than the statutorily mandated ceiling price, we could be subject to significant civil monetary penalties and/or such failure also could be grounds for HRSA to terminate our agreement to participate in the 340B program, in which case our covered outpatient drugs would no longer be eligible for federal payment under the Medicaid or Medicare Part B program, which would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including our ability to acquire, in-license or develop new products to grow our business. Moreover, HRSA established an ADR process under a final regulation for claims by covered entities that a manufacturer engaged in overcharging, including claims that a manufacturer limited the ability of a covered entity to purchase the manufacturer's drugs at the 340B ceiling price, and by manufacturers that a covered entity violated the prohibitions against diversion or duplicate discounts. Such claims are to be resolved through an ADR panel of government officials rendering a decision that may be appealed to a federal court. An ADR proceeding could potentially subject us to discovery by covered entities and other onerous procedural requirements and could result in additional liability. Additionally, HRSA issued a final rule that changes aspects of the ADR process effective June 2024, which could negatively affect us. In addition, HRSA could decide to terminate a manufacturer's agreement to participate in the 340B program for a violation of that agreement or other good cause shown, in which case the manufacturer's covered outpatient drugs may no longer be eligible for federal payment under the Medicaid or Medicare Part B program.

Further, legislation may be introduced at the state or Federal level that, if passed, would, among other things, modify the requirements of the 340B program.

Medicare Part D generally provides coverage to enrolled Medicare patients for self-administered drugs (*i.e.*, drugs that are not administered by a physician). Medicare Part D is administered by private prescription drug plans approved by the U.S. government and, subject to detailed program rules and government oversight, each drug plan establishes its own Medicare Part D formulary for prescription drug coverage and pricing, which the drug plan may modify from time to time. The prescription drug plans negotiate pricing with manufacturers and pharmacies and may condition formulary placement on the availability of manufacturer discounts. In addition, manufacturers, including us, were required through December 31, 2024 to provide to CMS a 70% discount on brand name prescription drugs utilized by Medicare Part D beneficiaries when those beneficiaries are in the coverage gap phase of the Part D benefit design. Civil monetary penalties could be due if we fail to offer discounts to beneficiaries under the Medicare Part D coverage gap discount program. The IRA sunsets the coverage gap discount program starting in 2025 and replaces it with a new manufacturer discount program, under which manufacturers are, in general, to provide a 10% discount on a covered Part D drug where a beneficiary is in the initial phase of Part D coverage and a 20% discount where a beneficiary is in the catastrophic phase of Part D coverage. Failure to pay a discount under this new program will be subject to a civil monetary penalty. In addition, the IRA established a Medicare Part D inflation rebate scheme, under which, generally speaking, manufacturers will owe additional rebates if the average manufacturer price of a Part D drug increases faster than the pace of inflation. Failure to timely pay a Part D inflation rebate is subject to a civil monetary penalty.

The IRA also creates a drug price negotiation program under which the prices for Medicare units of certain high Medicare spend drugs and biologicals without generic or biosimilar competition will be capped by reference to, among other things, a specified non-federal average manufacturer price starting in 2026. Failure to comply with requirements under the drug price negotiation program is subject to an excise tax and/or a civil monetary penalty. This or any other legislative change could impact the market conditions for our products. We further expect continued scrutiny on government price reporting from Congress, agencies, and other bodies.

Pursuant to applicable law, knowing provision of false information in connection with price reporting under the U.S. Department of Veterans Affairs, FSS or Tricare programs can subject a manufacturer to civil monetary penalties. These program obligations also contain extensive disclosure and certification requirements. If we overcharge the government in connection with our arrangements with FSS or Tricare, we are required to refund the difference to the government. Failure to make necessary disclosures and/or to identify contract overcharges can result in allegations against us under the False Claims Act and other laws and regulations. Unexpected refunds to the government, and responding to a government investigation or enforcement action, would be expensive and time-consuming, and could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Product liability and product recalls could harm our business.

The development, manufacture, testing, marketing and sale of pharmaceutical products are associated with significant risks of product liability claims or recalls. Side effects or adverse events known or reported to be associated with, or manufacturing defects in, the products sold by us could exacerbate a patient's condition, or could result in serious injury or impairment or even death. This could result in product liability claims against us and/or recalls of one or more of our products. In many countries, including in EU member states, national laws provide for strict (no-fault) liability which applies even where damages are caused both by a defect in a product and by the act or omission of a third party.

Product recalls may be issued at our discretion or at the discretion of our suppliers, government agencies and other entities that have regulatory authority for pharmaceutical sales. Any recall of our products could materially adversely affect our business by rendering us unable to sell that product for some time and by adversely affecting our reputation. A recall could also result in product liability claims by individuals and third party payors. In addition, product liability claims could result in an investigation of the safety or efficacy of our products, our manufacturing processes and facilities, or our marketing programs conducted by FDA, the EC or the competent authorities of the EU member states. Such investigations could also potentially lead to a recall of our products or more serious enforcement actions, limitations on the therapeutic indications for which they may be used, or suspension, variation, or withdrawal of approval. Any such regulatory action by FDA, the EC or the competent authorities of the EU member states could lead to product liability lawsuits as well.

Product liability insurance coverage is expensive, can be difficult to obtain and may not be available in the future on acceptable terms, or at all. Our product liability insurance may not cover all of the future liabilities we might incur in connection with the development, manufacture or sale of our products. A successful claim or claims brought against us in excess of available insurance coverage could subject us to significant liabilities and could have a material adverse effect on our business, financial condition, results of operations and growth prospects. Such claims could also harm our reputation and the reputation of our products, adversely affecting our ability to market our products successfully.

We use hazardous materials in our manufacturing facilities, and any claims relating to the improper handling, storage, release or disposal of these materials could be time-consuming and expensive.

Our operations are subject to complex and increasingly stringent environmental, health and safety laws and regulations in the countries where we operate and, in particular, in Ireland, the U.K. and Italy where we have manufacturing facilities. If an accident or contamination involving pollutants or hazardous substances occurs, an injured party could seek to hold us liable for any damages that result and any liability could exceed the limits or fall outside the coverage of our insurance. We may not be able to maintain insurance with sufficient coverage on acceptable terms, or at all. Costs, damages and/or fines may result from the presence, investigation and remediation of such contamination at properties currently or formerly owned, leased or operated by us or at off-site locations, including where we have arranged for the disposal of hazardous substances or waste. In addition, we may be subject to third party claims, including for natural resource damages, personal injury and property damage, in connection with such contamination.

Risks Related to Controlled Substances

Xyrem and Xywav are controlled substances and certain product candidates we are developing may be subject to U.S. federal and state controlled substance laws and regulations, and our failure to comply with these laws and regulations, or the cost of compliance with these laws and regulations, could materially and adversely affect our business, results of operations, financial condition and growth prospects.

Xyrem and Xywav and certain product candidates we are developing contain controlled substances as defined by state law and the federal CSA. Controlled substances are subject to a number of requirements and restrictions under the CSA and implementing regulations, including certain registration, security, recordkeeping, reporting, import, export and other requirements administered by the DEA. The DEA classifies controlled substances into five schedules: Schedule I, II, III, IV or V substances. Schedule I substances by definition have a high potential for abuse, no currently "accepted medical use" in the U.S., lack accepted safety for use under medical supervision, and may not be prescribed, marketed or sold in the U.S. Pharmaceutical products approved for use in the U.S. which contain a controlled substance are listed as Schedule II, III, IV or V, with Schedule II substances considered to present the highest potential for abuse or dependence and Schedule V substances the lowest relative risk of abuse among such substances. Schedule I and II drugs are subject to the strictest controls under the CSA, including manufacturing and procurement quotas, heightened security requirements and additional criteria for importation. In addition, dispensing of Schedule II drugs is subject to additional requirements. For example, they may not be refilled without a new prescription.

Drug products approved for medical use by FDA that contain cannabis or cannabis extracts may be controlled substances and will be rescheduled to Schedules II-V after approval, or, like Epidiolex, removed completely from the schedules by operation of other laws.

Individual states have also established controlled substance laws and regulations. Though state-controlled substances laws often mirror federal law, they may separately schedule our products or our product candidates as well. We or our partners may also be required to obtain separate state registrations, permits or licenses in order to be able to manufacture, distribute, administer or prescribe controlled substances for clinical trials or commercial sale, and failure to meet applicable regulatory requirements could lead to enforcement and sanctions by the states in addition to those from the DEA or otherwise arising under federal law.

U.S. facilities conducting research, manufacturing, distributing, importing or exporting, or dispensing controlled substances must be registered (licensed) to perform these activities and must comply with the security, control, recordkeeping and reporting obligations under the CSA, DEA regulations and corresponding state requirements. DEA and state regulatory bodies conduct periodic inspections of certain registered establishments that handle controlled substances. Obtaining and maintaining the necessary registrations and complying with the regulatory obligations may result in delay of the importation, manufacturing, distribution or clinical research of our commercial products and product candidates. Furthermore, failure to maintain compliance with the CSA and DEA and state regulations by us or any of our contractors, distributors or pharmacies can result in regulatory action that could have a material adverse effect on our business, financial condition and results of operations. DEA and state regulatory bodies may seek civil penalties, refuse to renew necessary registrations, or initiate proceedings to restrict, suspend or revoke those registrations. In certain circumstances, violations could lead to criminal penalties.

Schedule I and II substances are subject to DEA's annual manufacturing and procurement quota requirements. The annual quota allocated to us or our contract manufacturers for the active ingredients in our products may not be sufficient to complete clinical trials or meet commercial demand. Consequently, any delay or refusal by the DEA in establishing our, or our contract manufacturers', procurement and/or production quota for controlled substances could delay or stop our clinical trials or product launches, which could have a material adverse effect on our business, results of operations, financial condition and growth prospects.

Our ability to research, develop and commercialize Epidiolex/Epidyolex is dependent on our ability to maintain licenses relating to the cultivation, possession and supply of botanical cannabis, a controlled substance.

Our cannabinoid research and manufacturing facilities are located predominantly in the U.K. In the U.K., licenses to cultivate, possess and supply cannabis for medical research are granted by the U.K. government on an annual basis. Although our licenses have been renewed each year since 1998, they may not be in the future, in which case we may not be able to carry on our research and development program in the U.K. In addition, we are required to maintain our existing commercial licenses to cultivate, produce and supply cannabis. However, if the U.K. government were not prepared to renew such licenses, we would be unable to manufacture and distribute our products on a commercial basis in the U.K. or beyond. In order to carry out research in countries other than the U.K., similar licenses to those outlined above are required to be issued by the relevant authority in each country. In addition, we will be required to obtain licenses to export from the U.K. and to import into the recipient country. To date, we have obtained necessary import and export licenses to over 30 countries. Although we have an established track record of successfully obtaining such licenses as required, this may change in the future, which could materially and adversely affect our business, results of operations, financial condition and growth prospects.

Controlled substance legislation differs between countries and legislation in certain countries may restrict or limit our ability to sell Epidyolex.

Most countries are parties to the Single Convention on Narcotic Drugs 1961, which governs international trade and domestic control of narcotic substances, including cannabis extracts. Countries may interpret and implement their treaty obligations in a way that creates a legal obstacle to our obtaining regulatory approval for Epidyolex in those countries. These countries may not be willing or able to amend or otherwise modify their laws and regulations to permit Epidyolex to be marketed, or achieving such amendments to the laws and regulations may take a prolonged period of time.

Risks Related to Our Financial Condition and Results

We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.

As of December 31, 2024, we had total indebtedness of approximately \$6.2 billion. Our substantial indebtedness may:

- limit our ability to use our cash flow or borrow additional funds for working capital, capital expenditures, acquisitions, investments or other general business purposes;
- require us to use a substantial portion of our cash flow from operations to make debt service payments;
- limit our flexibility to plan for, or react to, changes in our business and industry, or our ability to take specified actions to take advantage of certain business opportunities that may be presented to us;

- expose us to the risk of increased interest rates as certain of our borrowings, including a portion of borrowings under the Amended Credit Agreement, are at variable rates of interest;
- result in dilution to our existing shareholders to the extent that the remainder, if any, of the exchange obligation in excess of our Exchangeable Senior Notes are settled in our ordinary shares upon exchange;
- place us at a competitive disadvantage compared to our less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay investments and capital expenditures, seek additional capital or restructure or refinance our debt. These alternative measures may not be successful and may not permit us to meet our debt service obligations. In the absence of such cash flows and resources, we could face substantial liquidity problems and might be required to dispose of material assets or operations to meet our debt service and other obligations. In addition, if we are unable to repay amounts under our Amended Credit Agreement or Secured Notes, the Amended Credit Agreement lenders and note holders could proceed against the collateral granted to them to secure that debt, which would seriously harm our business.

Covenants in the Amended Credit Agreement and indenture governing our Secured Notes restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

The Amended Credit Agreement and the indenture governing our Secured Notes contain various covenants that, among other things, limit our ability and/or our restricted subsidiaries' ability to:

- incur or assume liens or additional debt or provide guarantees in respect of obligations of other persons;
- pay dividends or distributions or redeem or repurchase capital stock;
- prepay, redeem or repurchase certain debt;
- make loans, investments, acquisitions (including certain acquisitions of exclusive licenses) and capital expenditures;
- enter into agreements that restrict distributions from our subsidiaries;
- enter into transactions with affiliates;
- enter into sale and lease-back transactions;
- sell, transfer or exclusively license certain assets, including material intellectual property, and capital stock of our subsidiaries; and
- consolidate or merge with or into, or sell substantially all of our assets to, another person.

If we undergo a change of control triggering event, we would be required to make an offer to purchase all of the Secured Notes at a purchase price in cash equal to 101% of their principal amount, plus accrued and unpaid interest, subject to certain exceptions. If we engage in certain asset sales, we will be required under certain circumstances to make an offer to purchase the Secured Notes at 100% of the principal amount, plus accrued and unpaid interest.

The Amended Credit Agreement also includes certain financial covenants that require us to maintain a maximum secured leverage ratio and a minimum interest coverage ratio as long as we have drawn funds under the Amended Revolving Credit Facility (or letters of credit in excess of \$50 million have been issued and remain undrawn).

As a result of these restrictions, we may be:

- limited in how we conduct our business;
- unable to raise additional debt or equity financing to operate during general economic or business downturns; or
- unable to compete effectively, take advantage of new business opportunities or grow in accordance with our plans.

Our failure to comply with any of the covenants could result in a default under the Amended Credit Agreement and the indenture governing our Secured Notes, which, if not cured or waived, could result in us having to repay our borrowings before their due dates. Such default may allow the lenders or the note holders to accelerate the related debt and may result in the acceleration of any other debt to which a cross-acceleration or cross-default provision applies. If we are forced to refinance these borrowings on less favorable terms or if we were to experience difficulty in refinancing the debt prior to maturity, our results of operations or financial condition could be materially affected. In addition, an event of default under the Amended Credit Agreement may permit the lenders to refuse to permit additional borrowings under the Amended Revolving Credit Facility or to terminate all commitments to extend further credit under the Amended Revolving Credit Facility. Furthermore, if we are unable to repay the amounts due and payable under the Amended Credit Agreement or the Secured Notes, as the case

may be, the lenders and note holders thereof may be able to proceed against the collateral granted to them to secure that indebtedness. In the event our lenders or note holders, as the case may be, accelerate the repayment of such borrowings, we cannot assure you that we will have sufficient assets to repay such indebtedness.

A default under the indentures governing our Exchangeable Senior Notes could also lead to a default under other debt agreements or obligations, including the Amended Credit Agreement and indenture governing the Secured Notes. Likewise, a default under the Amended Credit Agreement or the Secured Notes could lead to a default under other debt agreements or obligations, including the indentures governing our Exchangeable Senior Notes.

To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate and grow our business.

The scope of our business and operations has grown substantially, including through a series of business combinations and acquisitions. To continue to grow our business over the longer term, we plan to commit substantial resources to product acquisition and in-licensing, product development, clinical trials of product candidates and expansion of our commercial, development, manufacturing and other operations. Acquisition opportunities that we pursue could materially affect our liquidity and capital resources and may require us to incur additional indebtedness, seek equity capital or both. Our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures, potential future bank failures or otherwise. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital, and we currently have such authorization. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro-rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2024, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation. This current pre-emption opt-out authority is due to expire in January 2026. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital, could be adversely affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities and could otherwise have a material adverse effect on our business and growth prospects. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose.

We have significant intangible assets and goodwill. Consequently, the future impairment of our intangible assets and goodwill may significantly impact our profitability.

Our intangible assets and goodwill are significant and are subject to an impairment analysis whenever events or changes in circumstances indicate the carrying amount of the asset may not be recoverable. Additionally, goodwill and indefinite-lived assets are subject to an impairment test at least annually. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. For example, in the third quarter of 2022, we recorded a \$133.6 million asset impairment charge as a result of the decision to discontinue our nabiximols program. Our results of operations and financial position in future periods could be negatively impacted should future impairments of intangible assets or goodwill occur.

Our financial results have been and may continue to be adversely affected by foreign currency exchange rate fluctuations.

Because our financial results are reported in U.S. dollars, we are exposed to foreign currency exchange risk as the functional currency financial statements of non-U.S. subsidiaries are translated to U.S. dollars for reporting purposes. To the extent that revenue and expense transactions are not denominated in the functional currency, we are also subject to the risk of transaction losses. For example, because our product sales outside of the U.S. are primarily denominated in the euro, our sales of those products have been and may continue to be adversely affected by fluctuations in foreign currency exchange rates. Given the volatility of exchange rates, as well as our expanding operations, there is no guarantee that we will be able to effectively manage currency transaction and/or translation risks, which could adversely affect our operating results. Although we utilize foreign exchange forward contracts to manage currency risk primarily related to certain intercompany balances denominated in non-functional currencies, our efforts to manage currency risk may not be successful.

Changes in our effective tax rates could adversely affect our business and financial condition, results of operations and growth prospects.

We are incorporated in Ireland and maintain subsidiaries in North America, the U.K. and a number of other foreign jurisdictions. As a result, our effective tax rate is derived from a combination of applicable tax rates in the various jurisdictions where we operate. Our effective tax rate may fluctuate depending on a number of factors, including, but not limited to, the

distribution of our profits or losses between the jurisdictions where we operate and changes to or differences in interpretation of tax laws. For example, our income tax expense for the year ended December 31, 2021, included an expense of \$259.9 million arising on the remeasurement of our U.K. net deferred tax liability, which arose primarily in relation to the GW Acquisition, due to a change in the statutory tax rate in the U.K. following enactment of the U.K. Finance Act 2021.

We are subject to reviews and audits by the U.S. IRS, and other taxing authorities from time to time, and the IRS or other taxing authority may challenge our structure, transfer pricing arrangements and tax positions through an audit or lawsuit. Responding to or defending against challenges from taxing authorities could be expensive and consume time and other resources. If we are unsuccessful, we may be required to pay additional taxes for prior periods, interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our products or seek to raise additional funds. Any of these actions could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Changes to tax laws relating to multinational corporations could adversely affect us.

The U.S. Congress, the EU, the OECD, and other government agencies in jurisdictions where we and our affiliates do business have had an extended focus on issues related to the taxation of multinational corporations. As a result of the focus on the taxation of multinational corporations, the tax laws in Ireland, the U.S. and other countries in which we and our affiliates do business could change on a prospective or retroactive basis, and any such changes could adversely affect us.

One example is the OECD's initiative in the area of "base erosion and profit shifting." In October 2021, the OECD released Pillar Two. In December 2022, the EU agreed to implement this global minimum tax rate for EU member states by the start of 2024. In accordance with the EU directive, Ireland adopted legislation implementing Pillar Two on December 18, 2023, with effect from the start of 2024. Other jurisdictions in which we do business have also adopted legislation implementing Pillar Two. Pillar Two legislation could have an adverse impact on our effective tax rate, tax liabilities, and cash tax.

Further, the IRA, among other things, introduced new tax provisions, including a 15% corporate alternative minimum tax for certain large corporations, and a one percent excise tax on certain share repurchases by publicly traded corporations, including certain repurchases by specified domestic affiliates of publicly traded foreign corporations. These provisions became effective in 2023. The IRS has issued limited guidance on the corporate alternative minimum tax, the excise tax and the other tax provisions in the IRA, and much of this guidance has yet to be finalized. Final guidance under the IRA could adversely affect our tax provision, cash tax liability and effective tax rate.

The U.S. and other jurisdictions in which we operate continue to consider other changes in tax laws and regulations that apply to multinationals, including proposed legislation and guidance with respect to research and development expenditures and other guidance under the 2017 Tax Cuts and Jobs Act. The new presidential administration has included as part of its agenda a potential reform of U.S. tax laws, the details of which have not yet emerged. In addition, certain of the provisions in the 2017 Tax Cuts and Jobs Act will change or expire on December 31, 2025 unless Congress takes action to extend these provisions in their current form. In particular, a significant portion of our income taxable in the U.S. qualifies for preferential treatment as foreign-derived intangible income. Beginning in 2026, the effective tax rate for foreign-derived intangible income will increase from 13% to 16%. If U.S. tax rates increase and/or the foreign-derived intangible income deduction is reduced or eliminated, our tax provision, cash tax liability and effective tax rate would be adversely affected.

The IRS may not agree with the conclusion that we should be treated as a foreign corporation for U.S. federal tax purposes.

Although we are incorporated in Ireland, the IRS may assert that we should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal tax purposes pursuant to Section 7874 of the Code. For U.S. federal tax purposes, a corporation generally is considered a tax resident in the jurisdiction of its organization or incorporation. Because we are an Irish incorporated entity, we would be classified as a foreign corporation (and, therefore, a non-U.S. tax resident) under these rules. Section 7874 of the Code provides an exception under which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal tax purposes. Because we indirectly acquired all of Jazz Pharmaceuticals, Inc.'s assets through the acquisition of the shares of Jazz Pharmaceuticals, Inc. common stock when the businesses of Jazz Pharmaceuticals, Inc. and Azur Pharma Public Limited Company were combined in the Azur Merger, the IRS could assert that we should be treated as a U.S. corporation for U.S. federal tax purposes under Section 7874. Moreover, new statutory and/or regulatory provisions under Section 7874 of the Code or otherwise could be enacted that could adversely affect our status as a foreign corporation for U.S. federal tax purposes, and any such provisions could have prospective or retroactive application to us, our shareholders, Jazz Pharmaceuticals, Inc. and/or the Azur Merger.

Our ability to use NOLs and carryforward tax losses to offset potential taxable income is limited under applicable law and could be subject to further limitations if we do not generate taxable income in a timely manner or if certain “ownership change” provisions of applicable law result in further limitations.

Our ability to use NOLs to offset potential future taxable income and related income taxes that would otherwise be due also depends on our ability to generate future income that is taxable in the U.S. before the NOLs expire. We cannot predict with certainty when, or whether, our U.S. affiliates will generate sufficient taxable income to use all of the NOLs. In addition, the use of NOLs to offset potential future taxable income and related income taxes that would otherwise be due is subject to limitations under the “ownership change” provisions of Sections 382 and 383 of the Code and similar state provisions. Additionally, U.K. carryforward tax losses may become subject to limitations in the event of certain changes in the ownership interest of significant shareholders where there is also a major change in the nature of conduct of a trade or business within a specified period of time. These limitations may cause us to lose or forfeit additional NOLs or carryforward tax losses before we can use these attributes. Subsequent ownership changes and changes to the U.S. federal or state or U.K. tax rules with respect to the use of NOLs and carryforward tax losses may further affect our ability to use these losses in future years.

Risks Related to Our Ordinary Shares

The market price of our ordinary shares has been volatile and is likely to continue to be volatile in the future, and the value of your investment could decline significantly.

The stock market in general, including the market for life sciences companies, has experienced extreme price and trading volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies, which has resulted in decreased market prices, notwithstanding the lack of a fundamental change in the underlying business models of those companies. Worsening economic conditions and other adverse effects or developments may negatively affect the market price of our ordinary shares, regardless of our actual operating performance. The market price for our ordinary shares is likely to continue to be volatile and subject to significant price and volume fluctuations in response to market, industry and other factors, including the risk factors described in this “Risk Factors” section.

Our share price may be dependent upon the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts’ forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, the market price of our ordinary shares could decline. Our ability to meet analysts’ forecasts, investors’ expectations and our financial guidance is substantially dependent on our ability to maintain or increase sales of our marketed products.

In addition, the market price of our ordinary shares may decline if the effects of our strategic transactions on our financial or operating results are not consistent with the expectations of financial analysts or investors. The market price of our ordinary shares could also be affected by possible sales of our ordinary shares by holders of our Exchangeable Senior Notes who may view our Exchangeable Senior Notes as a more attractive means of equity participation in our company and by hedging or arbitrage trading activity involving our ordinary shares by the holders of our Exchangeable Senior Notes.

We are subject to Irish law, which differs from the laws in effect in the U.S. and may afford less protection to holders of our securities.

It may not be possible to enforce court judgments obtained in the U.S. against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liability provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the U.S. currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically be enforceable in Ireland.

As an Irish company, we are governed by the Irish Companies Act 2014, which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions, mergers, amalgamations and acquisitions, takeovers and shareholder lawsuits. The duties of directors and officers of an Irish company are generally owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a U.S. jurisdiction.

Our articles of association, Irish law, the Amended Credit Agreement and the indentures governing our Secured Notes and Exchangeable Senior Notes contain provisions that could delay or prevent a takeover of us by a third party.

Our articles of association could delay, defer or prevent a third party from acquiring us, despite the possible benefit to our shareholders, or otherwise adversely affect the price of our ordinary shares. In addition to our articles of association, several mandatory provisions of Irish law could prevent or delay an acquisition of us. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our shares in certain circumstances. Furthermore, a takeover of us may trigger a default under the Amended Credit Agreement or the requirement that we offer to purchase our Secured Notes or Exchangeable Senior Notes and/or increase the exchange rate applicable to our Exchangeable Senior Notes, which could make it more costly for a potential acquirer to engage in a business combination transaction with us.

These provisions, whether alone or together, may discourage potential takeover attempts, discourage bids for our ordinary shares at a premium over the market price or adversely affect the market price of, and the voting and other rights of the holders of, our ordinary shares. These provisions, whether alone or together, could also discourage proxy contests and make it more difficult for our shareholders to elect directors other than the candidates nominated by our board.

Future sales and issuances of our ordinary shares, securities convertible into or exercisable or exchangeable for our ordinary shares or rights to purchase ordinary shares or convertible or exchangeable securities could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to decline.

We expect to continue to opportunistically seek access to additional capital to license or acquire additional products, product candidates or companies to expand our operations or for general corporate purposes. To the extent we raise additional capital by issuing equity securities or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted.

We have never declared or paid dividends on our capital stock and we do not anticipate paying dividends in the foreseeable future.

We do not currently plan to pay cash dividends in the foreseeable future. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, compliance with the terms of the Amended Credit Agreement and the indenture governing our Secured Notes, and other factors our board of directors deems relevant. Accordingly, holders of our ordinary shares must rely on increases in the trading price of their shares for returns on their investment in the foreseeable future. In addition, in the event that we pay a dividend on our ordinary shares, in certain circumstances, as an Irish tax resident company, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

General Risk Factors

If we fail to attract, retain and motivate members of our executive management team and key personnel, our operations and our future growth may be adversely affected.

Our success and our ability to grow depend in part on our continued ability to attract, retain and motivate highly qualified personnel, including our executive management team. In addition, changes we make to our current and future work environments may not meet the needs or expectations of our employees or may be perceived as less favorable compared to other companies' policies, which could negatively impact our ability to hire and retain qualified personnel, whether in a remote or in-office environment. In December 2024, our Chief Executive Officer notified us of his intent to retire from his role as Chief Executive Officer upon the selection and appointment of our next Chief Executive Officer, and to continue serving as Chairperson of the Board of Directors. Moreover, the loss of services and institutional knowledge of one or more additional members of our executive management team or other key personnel could delay or prevent the successful completion of some of our vital activities and may negatively impact our operations and future growth. We do not carry "key person" insurance. In addition, changes in our organization as a result of executive management transition may have a disruptive impact on our ability to implement our strategy. Until we integrate new personnel, and unless they are able to succeed in their positions, we may be unable to successfully manage and grow our business. In any event, if we are unable to attract, retain and motivate quality individuals, or if there are delays, or if we do not successfully manage personnel and executive management transitions, our business, financial condition, results of operations and growth prospects could be adversely affected.

Anti-diversity, equity and inclusion initiatives could expose us to the risk of litigation or investigations, resulting in injunctions, penalties, or reputational harm.

We have talent management efforts designed to build and maintain an inclusive environment with diverse thought, backgrounds, experiences and skillsets throughout our organization. However, there has been increasing scrutiny on corporate DEI initiatives, including from activists and policymakers challenging how such initiatives comply with civil rights protections. For example, the U.S. President recently issued an executive order opposing DEI initiatives in the private sector. Such anti-DEI initiatives and scrutiny could expose us to the risk of litigation or investigations, resulting in injunctions, penalties, or reputational harm. In addition, if we become unable to (or are perceived not to) successfully implement certain of our workforce initiatives, including in keeping with current or potential future laws or interpretations thereof, our ability to recruit, attract and retain talent may be adversely impacted.

Our business and operations could be negatively affected if we become subject to shareholder activism or hostile bids, which could cause us to incur significant expense, hinder execution of our business strategy and impact our stock price.

Shareholder activism, which takes many forms and arises in a variety of situations, has been increasingly prevalent. Stock price declines may also increase our vulnerability to unsolicited approaches. If we become the subject of certain forms of shareholder activism, such as proxy contests or hostile bids, the attention of our management and our board of directors may be diverted from execution of our strategy. Such shareholder activism could give rise to perceived uncertainties as to our future strategy, adversely affect our relationships with business partners and make it more difficult to attract and retain qualified personnel. Also, we may incur substantial costs, including significant legal fees and other expenses, related to activist shareholder matters. Our stock price could be subject to significant fluctuation or otherwise be adversely affected by the events, risks and uncertainties of any shareholder activism.

Item 1B. Unresolved Staff Comments

There are no material unresolved written comments that were received from the SEC staff 180 days or more before the end of our 2024 fiscal year relating to our periodic or current reports under the Securities Exchange Act of 1934, as amended.

Item 1C. Cybersecurity

Risk management and strategy

We have implemented and maintain an information security program designed to identify, assess, and manage material risks from cybersecurity threats to our critical computer networks, third party hosted services, communications systems, hardware and software, and our critical data including intellectual property, clinical trial participant and patient-related data, and confidential information that is proprietary, strategic or competitive in nature, or collectively, Information Systems and Data.

Our cybersecurity threat risk management processes include the following, among others:

- Our information security department identifies and assesses risks from cybersecurity threats by monitoring and evaluating our threat environment and risk profile using various methods including, for example, manual methods and automated tools, conducting scans of the threat environment, conducting threat assessments, performing vulnerability assessments, use of external intelligence feeds, and through third-party-conducted red/blue team testing and tabletop incident response exercises.
- Depending on the environment, we implement and maintain various technical, physical and organizational measures, processes, standards and policies designed to manage and mitigate material risks from cybersecurity threats to our Information Systems and Data, including, for example: information security policies and standards governing access control, network and device security, encryption standards, incident response plans, disaster recovery plans, risk management, vulnerability detection and management and security awareness training requirements as well as security tools such as firewalls, malware protection tools, secure authentication tools, centralized logging and monitoring tools, threat intelligence tools, and data protection tools.
- Our overall risk assessment and management processes address cybersecurity threats that may have a material impact on our business. Our information security department maintains a risk register of individual risks from cybersecurity threats. Our CISO and CIO periodically review the area of cybersecurity risk management within our overall enterprise risk management program and work with our executive director of internal audit and enterprise risk management to incorporate the aggregate risks from the cybersecurity threat risk register into the overall enterprise risk management program risk register. In addition, our CISO and CIO report significant increases to our threat profile to the Information Security Governance Committee (described below).

- We use third parties, including professional services, incident response and managed security firms (including some that we have on a pre-paid retainer basis), to assist us from time to time to identify, assess, and manage cybersecurity risks, perform threat assessments relating to our Information Systems and Data by reviewing our business and industry vertical threat profiles and applying those to the overall threat landscape, perform penetration tests, conduct cybersecurity readiness exercises, assess program maturity, and to assist in the event of a cyber security incident.
- We have third-party vendor management processes designed to help us identify, assess and manage risks from cybersecurity threats to our Information Systems and Data that may arise out of our use of third-party vendors across our business, including, among others, application providers, hosting companies, contract research organizations, contract manufacturing organizations, distributors, and supply chain resources. Depending on the nature of the services and the service provider, our vendor management processes may include assessment of the cybersecurity practices of such vendors and contractually imposing obligations on the provider.

For a description of the risks from cybersecurity threats that may materially affect us and how those risks may affect us see “*Significant disruptions of information technology systems or data security breaches could adversely affect our business*” under Part I, Item 1A. Risk Factors in this Annual Report on Form 10-K.

Governance

- Our board of directors addresses our cybersecurity risk management as part of its general oversight function. The Audit Committee helps oversee our cybersecurity risk management processes, including oversight of risks from cybersecurity threats.
- The Information Governance Security Committee and the Audit Committee receive various reports from CISO and CIO. The CISO (or its designee) reports to the Audit Committee on cybersecurity risk on at least a quarterly basis. Written reports and presentation materials regarding cybersecurity risk provided to the Audit Committee are made available to the board of directors and they can discuss the materials and cybersecurity risk with the Audit Committee members. The Internal Audit team oversees internal controls implemented by us under our information security program.
- Our information security program is implemented and maintained by certain of our management, including the CISO, CIO and other members of our Information Security Governance Committee (Chief Legal Officer, Chief Financial Officer, and Chief Privacy Officer).
- The Information Security Governance Committee helps assess and manage our cybersecurity risks and monitor the effectiveness of our information security program and risk management. Management, including those serving on our Information Security Governance Committee, is responsible for hiring appropriate cybersecurity personnel, helping to integrate cybersecurity considerations into our overall risk management strategy, providing appropriate resources for cybersecurity risk management, and communicating key priorities to relevant personnel. Our cybersecurity incident response plan includes processes designed to escalate certain cybersecurity incidents that caused a significant impact to us to members of the Information Security Governance Committee, and certain members of executive management depending on the circumstances. In addition, our incident response plan includes reporting to the Audit Committee for certain cybersecurity incidents, including those that have potentially had a material impact to us.

Item 2. Properties

Our corporate headquarters are located in Dublin, Ireland, and our U.S. operations are located in Palo Alto, California, Carlsbad, California and Philadelphia, Pennsylvania. In addition to our owned manufacturing and development facilities and our leased administrative, manufacturing and development facilities, we also have dedicated growing facilities operated by contract partners. The following table contains information about our significant properties as of December 31, 2024:

Type	Location	Approximate Square Feet	Lease / Contract Expiration Date
Administrative office	Dublin, Ireland	45,000	2036
Administrative office	Palo Alto, United States	99,000	2025
Administrative office	Philadelphia, United States	60,000	2029
Administrative office	Carlsbad, United States	43,000	2028
Administrative office	Oxford, United Kingdom	26,000	2025
Administrative office	Cambridge, United Kingdom	22,000	2030-2031
Administrative office and laboratory	Vancouver, Canada	15,000	2029
Administrative office	London, United Kingdom	13,000	2034
Administrative office and laboratory	Villa Guardia (Como), Italy	34,000	2029
Manufacturing and development	Athlone, Ireland	58,000	Owned
Manufacturing and development	Southern United Kingdom	136,000	2026-2036
Manufacturing and development	Villa Guardia (Como), Italy	45,000	Owned
Growing facility	Eastern United Kingdom	1,960,000	2026
Growing facility	Northern United Kingdom	915,000	2025
Growing facility	Southern United Kingdom	165,000	2028
Growing facility under construction	Southern United Kingdom	370,000	2035

In addition, we have offices in Japan, Australia, France and elsewhere in Europe.

On October 11, 2024, a new lease agreement was entered into for premises located at 3000 El Camino Real, Palo Alto, California, with an area of 27,000 square feet, with occupancy expected by July 1, 2025. The lease expires in 2035.

We believe that our existing properties are in good condition and suitable for the conduct of our business. As we continue to expand our operations, we may need to lease additional or alternative facilities.

Item 3. Legal Proceedings

The information required to be set forth under this Item 3 is incorporated by reference to Note 13, Commitments and Contingencies—Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K.

Item 4. Mine Safety Disclosures.

Not applicable.

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities**Market Information**

Our ordinary shares trade on The Nasdaq Global Select Market under the trading symbol "JAZZ."

Holders of Ordinary Shares

As of February 19, 2025, there were 882 holders of record of our ordinary shares. Because almost all of our ordinary shares are held by brokers, nominees and other institutions on behalf of shareholders, we are unable to estimate the total number of shareholders represented by these record holders.

Dividends

Under Irish law, dividends may only be paid, and share repurchases and redemptions must generally be funded only out of, "distributable reserves." In addition, the terms of the Amended Credit Agreement restrict our ability to make certain restricted payments, including dividends and other distributions by us in respect of our ordinary shares, subject to, among other exceptions, (1) a general exception for dividends and other restricted payments not to exceed in the aggregate the greater of \$350 million and 3.5% of consolidated total assets (as defined in the Amended Credit Agreement) when made, (2) an exception that allows for dividends and other restricted payments equal to an amount tied to our financial performance, so long as no default or event of default shall have occurred and is continuing under the Amended Credit Agreement and the total net leverage ratio (as defined in the Amended Credit Agreement) on a pro forma basis does not exceed 5:1, and (3) an exception that allows for additional dividends and other restricted payments, so long as no default or event of default shall have occurred and is continuing under the Amended Credit Agreement and the total net leverage ratio (as defined in our Amended Credit Agreement) on a pro forma basis is not greater than 4:1. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our consolidated financial condition, results of operations, capital requirements, compliance with the terms of the Amended Credit Agreement or other future borrowing arrangements, and other factors our board of directors deems relevant.

Irish Law Matters

As we are an Irish incorporated company, the following matters of Irish law are relevant to the holders of our ordinary shares.

Irish Restrictions on Import and Export of Capital

Except as indicated below, there are no restrictions on non-residents of Ireland dealing in Irish domestic securities, which includes ordinary shares of Irish companies. Dividends and redemption proceeds also continue to be freely transferable to non-resident holders of such securities. It is an offense under Irish law (pursuant to various statutory instruments) to transfer funds or make funds or economic resources available, directly or indirectly to any person or entity in contravention of Irish, EU or United Nations sanctions or to otherwise contravene Irish, EU or United Nations sanctions. Any transfer of, or payment in respect of, securities involving a person or entity that is currently the subject of Irish, EU or United Nations sanctions or any person or entity controlled by any of the foregoing, or any person acting on behalf of the foregoing, may be subject to restrictions pursuant to such sanctions as implemented into Irish law. The Financial Transfers Act, 1992 gives power to the Minister for Finance of Ireland to restrict financial transfers between Ireland and other countries and persons. Financial transfers are broadly defined and include all transfers that would be movements of capital or payments within the meaning of the treaties governing the member states of the EU. The acquisition or disposal of interests in shares issued by an Irish incorporated company and associated payments falls within this definition. In addition, dividends or payments on redemption or purchase of shares and payments on a liquidation of an Irish incorporated company would fall within this definition. The 1992 Act and underlying EU regulations prohibit financial transfers with certain persons and entities listed in the EU Consolidated Financial Sanctions List and United Nations Security Council Consolidated List, without the prior permission of the Central Bank of Ireland.

Any transfer of, or payment in respect of, a share or interest in a share involving the government of any country that is currently the subject of United Nations sanctions, any person or body controlled by any of the foregoing, or by any person acting on behalf of the foregoing, may be subject to restrictions pursuant to such sanctions as implemented into Irish law.

Irish Taxes Applicable to U.S. Holders

Irish Tax on Dividends. While we have no current plans to pay dividends, dividends on our ordinary shares would generally be subject to Irish Dividend Withholding Tax at the standard rate (currently 25%), unless an exemption applies.

Irish Tax on Capital Gains. A shareholder who (i) is neither resident nor ordinarily resident in Ireland for Irish tax purposes and (ii) does not use or hold, and did not acquire, our ordinary shares in connection with a trade or business carried on by such shareholder in Ireland through a branch or agency generally should not be subject to Irish tax on capital gains on a disposal of our ordinary shares.

A shareholder who is an individual and who is temporarily not resident in Ireland may, under Irish anti-avoidance legislation, still be liable for Irish tax on capital gains on any chargeable gain realized upon the disposal of our ordinary shares during the period in which such individual is a non-resident.

Capital Acquisitions Tax. Irish CAT is comprised principally of gift tax and inheritance tax. CAT could apply to a gift or inheritance of our ordinary shares irrespective of the place of residence, ordinary residence or domicile of the parties. This is because our ordinary shares are regarded as property situated in Ireland as our share register must be held in Ireland. The person who receives the gift or inheritance has primary liability for CAT.

CAT is levied at a rate of 33% above certain tax-free thresholds. The appropriate tax-free threshold is dependent upon (i) the relationship between the donor and the donee and (ii) the aggregation of the values of previous gifts and inheritances received by the donee from persons within the same category of relationship for CAT purposes. Gifts and inheritances passing between spouses are exempt from CAT. Our shareholders should consult their own tax advisers as to any tax consequences of holding our ordinary shares, including whether CAT is creditable or deductible in computing any domestic tax liabilities.

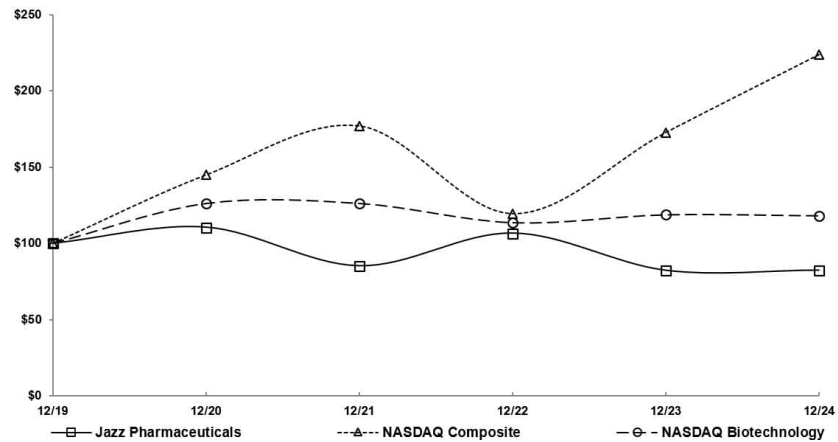
Stamp Duty. Irish stamp duty (if any) may become payable in respect of ordinary share transfers. However, a transfer of our ordinary shares from a seller who holds shares through DTC to a buyer who holds the acquired shares through DTC will not be subject to Irish stamp duty. A transfer of our ordinary shares (i) by a seller who holds ordinary shares outside of DTC to any buyer or (ii) by a seller who holds the ordinary shares through DTC to a buyer who holds the acquired ordinary shares outside of DTC, may be subject to Irish stamp duty (currently at the rate of 1% of the price paid or the market value of the ordinary shares acquired, if greater). The person accountable for payment of stamp duty is the buyer or, in the case of a transfer by way of a gift or for less than market value, all parties to the transfer.

A shareholder who holds ordinary shares outside of DTC may transfer those ordinary shares into DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) as a result of the transfer and at the time of the transfer into DTC there is no sale of those book-entry interests to a third party being contemplated by the shareholder. Similarly, a shareholder who holds ordinary shares through DTC may transfer those ordinary shares out of DTC without giving rise to Irish stamp duty provided that the shareholder would be the beneficial owner of the ordinary shares (and in exactly the same proportions) as a result of the transfer, and at the time of the transfer out of DTC there is no sale of those ordinary shares to a third party being contemplated by the shareholder. In order for the share registrar to be satisfied as to the application of this Irish stamp duty treatment where relevant, the shareholder must confirm to us that the shareholder would be the beneficial owner of the related book-entry interest in those ordinary shares recorded in the systems of DTC (and in exactly the same proportions) (or vice-versa) as a result of the transfer and there is no agreement being contemplated for the sale of the related book-entry interest or the ordinary shares or an interest in the ordinary shares, as the case may be, by the shareholder to a third party.

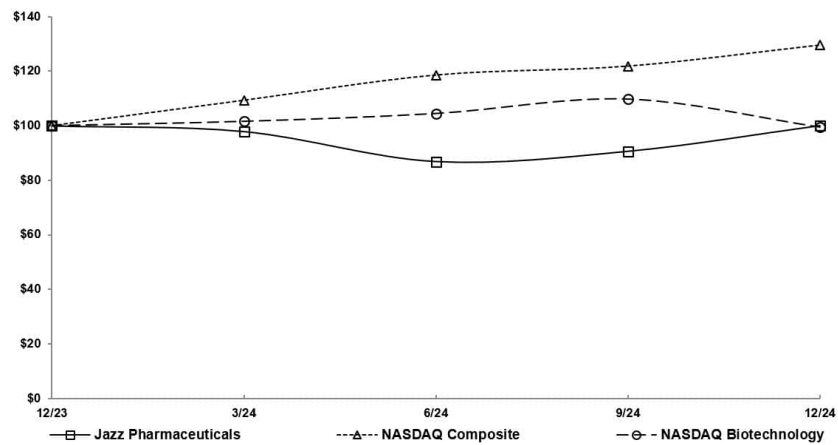
Performance Measurement Comparison (1)

The following graphs show the total shareholder return on the last day of each year of an investment of \$100 in cash as if made on December 31, 2019 and on the last day of each quarter of an investment of \$100 in cash as if made on December 31, 2023, respectively, in (i) our ordinary shares; (ii) the Nasdaq Composite Index; and (iii) the Nasdaq Biotechnology Index through December 31, 2024. The shareholder return shown in the graphs below are not necessarily indicative of future performance, and we do not make or endorse any predictions as to future shareholder returns.

COMPARISON OF FIVE YEAR CUMULATIVE TOTAL RETURN (2)



COMPARISON OF ONE YEAR CUMULATIVE TOTAL RETURN (2)



- (1) This section is not "soliciting material," is not deemed "filed" with the SEC and is not to be incorporated by reference into any of our filings under the Exchange Act, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing.
- (2) Information used in the graph was obtained from Research Data Group, Inc.

Issuer Purchases of Equity Securities

The following table summarizes purchases of our ordinary shares made by or on behalf of us or any of our “affiliated purchasers” as defined in Rule 10b-18(a)(3) under the Securities Exchange Act of 1934, as amended, during each fiscal month during the three-month period ended December 31, 2024:

	Total Number of Shares Purchased (1)	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs (2)	Maximum Number (or Approximate Dollar Value) of Shares that May Yet Be Purchased Under the Plans or Programs (3)
October 1 - October 31, 2024	—	\$ —	—	\$ 349,999,951
November 1 - November 30, 2024	—	\$ —	—	\$ 349,999,951
December 1 - December 31, 2024	—	\$ —	—	\$ 349,999,951
Total	—	\$ —	—	—

1. This table does not include ordinary shares that we withheld in order to satisfy tax withholding requirements in connection with the vesting and release of restricted stock units. No ordinary shares were otherwise repurchased during the three-month period ended December 31, 2024.
2. On July 31, 2024, we announced that our board of directors had authorized the use of up to \$500.0 million to repurchase our ordinary shares under the New Repurchase Program. Under the New Repurchase Program, which has no expiration date, we may repurchase ordinary shares from time to time by any methods and/or structures permitted by applicable law. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under our outstanding credit agreement and the indenture for our Secured Notes, corporate and regulatory requirements and market conditions. The New Repurchase Program may be modified, suspended or discontinued at any time without our prior notice. The ordinary shares reported in the table above were purchased pursuant to the New Repurchase Program. The New Repurchase Program replaces and supersedes the share repurchase program authorized by our board of directors in November 2016, which, as of July 25, 2024, the date it was replaced and superseded by the New Repurchase Program, had authorized the repurchase of ordinary shares having an aggregate purchase price of up to \$1.5 billion, exclusive of any brokerage commissions. On July 25, 2024, the amount remaining authorized for repurchase under the Old Repurchase Program was \$47,475, exclusive of any brokerage commissions, which amount is included in the \$500.0 million authorized for repurchase under the New Repurchase Program.
3. The dollar amount shown represents, as of the end of each period, the approximate dollar value of ordinary shares that may yet be purchased under the New Repurchase Program, exclusive of any brokerage commissions.

Item 6. Reserved**Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations**

The purpose of the Management Discussion and Analysis is to present information that management believes is relevant to promote an understanding of our results of operations and cash flows for the fiscal year ended December 31, 2024 and our financial condition as of December 31, 2024 and should be read in conjunction with the consolidated financial statements and notes to consolidated financial statements included elsewhere in this Annual Report on Form 10-K. This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that impact or could impact our business. In particular, we encourage you to review the risks and uncertainties described in “Risk Factors” in Part I, Item 1A in this Annual Report on Form 10-K. These risks and uncertainties could cause actual results to differ materially from those projected in forward-looking statements contained in this report or implied by past results and trends. Forward-looking statements are statements that attempt to forecast or anticipate future developments in our business, financial condition or results of operations. See the “Cautionary Note Regarding Forward-Looking Statements” that appears at the beginning of this Annual Report. These statements, like all statements in this report, speak only as of the date of this Annual Report on Form 10-K (unless another date is indicated), and we undertake no obligation to update or revise these statements in light of future developments. Forward-looking statements are statements that attempt to forecast or anticipate future developments in our business, financial condition or results of operations. See the “Cautionary Note Regarding Forward-Looking Statements” that appears at the beginning of this Annual Report. These statements, like all statements in this report, speak only as of the date of this Annual Report on Form 10-K (unless another date is indicated), and we undertake no obligation to update or revise these statements in light of future developments.

Overview

Jazz Pharmaceuticals plc is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases - often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience.

Our strategy for growth is rooted in executing commercial launches and ongoing commercialization initiatives, advancing robust R&D programs and delivering impactful clinical results, effectively deploying capital to strengthen the prospects of achieving our short- and long-term goals through strategic corporate development, and delivering strong financial performance. We focus on patient populations with high unmet needs. We seek to identify and develop differentiated therapies for these patients that we expect will be long-lived assets and that we can support with an efficient commercialization model. In addition, we leverage our efficient, scalable operating model and integrated capabilities across our global infrastructure to effectively reach patients around the world.

Our strategy to deliver sustainable growth and enhanced value continues to be focused on:

- Strong commercial execution to drive diversified revenue growth and address unmet medical needs of our patients across our product portfolio, which focuses on neuroscience and oncology medicines;
- Expanding and advancing our pipeline to achieve a valuable portfolio of durable, highly differentiated products;
- Continuing to build a flexible, efficient and productive development engine for targeted therapeutic areas to identify and progress early-, mid- and late-stage assets;
- Identifying and acquiring novel product candidates and approved therapies to complement our existing pipeline and commercial portfolio;
- Investing in an efficient, scalable operating model and differentiated capabilities to enable growth; and
- Unlocking further value through indication expansion and entry into global markets.

In 2024, consistent with our strategy, we continued to focus on research and development activities within our neuroscience and oncology therapeutic areas. For a summary of our ongoing research and development activities, see “Business—Research and Development” in Part I, Item 1 of this Annual Report on Form 10-K.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

Product	Indications	Initial Approval Date	Markets
NEUROSCIENCE			
Xywav® (calcium, magnesium, potassium, and sodium oxybates)	Treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy.	July 2020	U.S.
	Treatment of IH in adults.	August 2021	U.S.
	Treatment of cataplexy in patients with narcolepsy.	May 2023	Canada
Epidiolex® (cannabidiol)	Treatment of seizures associated with LGS, DS, or TSC in patients 1 year of age and older.	June 2018	U.S.
Epidyolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients 2 years of age and older. ¹	September 2019	EU, Great Britain, EEA, Israel, Switzerland, Australia and other markets
	For adjunctive therapy of seizures associated with TSC for patients 2 years of age and older.	April 2021	EU, Great Britain, Israel and Switzerland
Epidiolex® (cannabidiol)	For adjunctive therapy of seizures associated with LGS, DS or TSC for patients 2 years of age and older.	November 2023	Canada
ONCOLOGY			

<u>Product</u>	<u>Indications</u>	<u>Initial Approval Date</u>	<u>Markets</u>
Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL, and LBL, in adult and pediatric patients 1 month or older who have developed hypersensitivity to E. coli-derived asparaginase.	June 2021	U.S.
Rylaze® (crisantaspase recombinant)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL, in adults and pediatric patients 1 year or older who have developed hypersensitivity to E. coli-derived asparaginase.	September 2022	Canada
Enrylaze® (recombinant crisantaspase)	A component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL in adult and pediatric patients (1 month and older) who have developed hypersensitivity or silent inactivation to E. coli-derived asparaginase.	September 2023	EU, Great Britain, Switzerland, other markets
Zepzelca® (lurbinectedin)	Treatment of adult patients with metastatic SCLC, with disease progression on or after platinum-based chemotherapy.	June 2020	U.S. (licensed from PharmaMar) ²
	Treatment of adults with Stage III or metastatic SCLC who have progressed on or after platinum-containing therapy.	September 2021	Canada (licensed from PharmaMar) ³
Ziihera® (zanidatamab-hrii)	Treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.	November 2024	U.S. (licensed from Zymeworks) ²

¹The clobazam restriction limited to EU and Great Britain

² Accelerated approval received from FDA

³ Conditional approval received from Health Canada

Neuroscience

We are the global leader in the development and commercialization of oxybate therapy for patients with sleep disorders. Xyrem was approved by FDA in 2002, and is indicated for treating cataplexy and EDS in patients seven years of age or older with narcolepsy. In 2020, we received FDA approval for Xywav for the treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy. In August 2021, Xywav became the first and only therapy approved by FDA for the treatment of IH in adults. Xywav is an oxybate therapy that contains 92% less sodium than Xyrem. Xywav has become a standard of care for patients with narcolepsy and IH.

Since there is no cure for narcolepsy and long-term disease management is needed, we believe that Xywav represents an important therapeutic option for patients with this sleep disorder. Our commercial efforts are focused on educating patients and physicians about the lifelong impact of high sodium intake, and how the use of Xywav enables them to address what is a modifiable risk factor for cardiovascular morbidity. We view the adoption of Xywav in narcolepsy as a positive indication that physicians and patients appreciate the benefits of a low-sodium oxybate option.

In June 2021, FDA recognized seven years of ODE for Xywav in narcolepsy. ODE extends through January 2028. Nevertheless, Lumryz, a fixed-dose, high-sodium oxybate, was approved by FDA on May 1, 2023, for the treatment of cataplexy or EDS in adults with narcolepsy and was launched in the U.S. market by Avadel. FDA continues to recognize seven years of ODE for Xywav in narcolepsy. In connection with granting ODE, FDA stated that "Xywav is clinically superior to Xyrem by means of greater safety because Xywav provides a greatly reduced chronic sodium burden compared to Xyrem." FDA's summary also stated that "the differences in the sodium content of the two products at the recommended doses will be clinically meaningful in reducing cardiovascular morbidity in a substantial proportion of patients for whom the drug is indicated." FDA has also recognized that the difference in sodium content between Xywav and Lumryz is likely to be clinically meaningful in all patients with narcolepsy and that Xywav is safer than Lumryz in all such patients. Lumryz has the same sodium content as Xyrem. Xywav is the only approved oxybate therapy that does not carry a warning and precaution related to high sodium intake.

On August 12, 2021, FDA approved Xywav for the treatment of IH in adults. Xywav remains the first and only FDA-approved therapy to treat IH. We initiated the U.S. commercial launch of Xywav for the treatment of IH in adults in November 2021. In January 2022, FDA recognized seven years of ODE for Xywav in IH that extends through August 2028. IH is a debilitating neurologic sleep disorder characterized by chronic EDS (the inability to stay awake and alert during the day resulting in the irrepressible need to sleep or unplanned lapses into sleep or drowsiness), severe sleep inertia, and prolonged and non-restorative nighttime sleep. An estimated 37,000 people in the U.S. have been diagnosed with IH and are actively seeking healthcare.

We have agreements in place for Xywav with all three major PBMs in the U.S. To date, we have entered into agreements with various entities and have achieved benefit coverage for Xywav in both narcolepsy and IH indications for approximately 90% of commercial lives.

We have seen strong adoption of Xywav in narcolepsy since its launch in November 2020, and increasing adoption in IH since its launch in November 2021. Exiting 2024, there were approximately 14,150 patients taking Xywav, including approximately 10,250 patients with narcolepsy and approximately 3,900 patients with IH.

We acquired Epidiolex (Epidyolex outside the U.S.) in May 2021 as part of the GW Acquisition, which expanded our growing neuroscience business with a global, high-growth childhood-onset epilepsy franchise. Epidiolex was approved in the U.S. in June 2018 for the treatment of seizures associated with two rare and severe forms of epilepsy, LGS and DS, in patients two years of age and older, and subsequently approved in July 2020 for the treatment of seizures associated with TSC in patients one year of age and older. FDA also approved the expansion of all existing indications, LGS and DS, to patients one year of age and older. The rolling European launch of Epidyolex is also underway following EC approval in September 2019 for use as adjunctive therapy of seizures associated with LGS or DS, in conjunction with clobazam, for patients two years of age and older. The clobazam restriction is limited to the EU and Great Britain. Epidyolex is now launched in all five key European markets: United Kingdom, Germany, Italy, Spain and France. Epidyolex was also approved for adjunctive therapy of seizures associated with TSC for patients 2 years of age and older in the EU in April 2021 and Great Britain in August 2021, and is approved or under review for this indication in other markets. Outside the U.S. and Europe, Epidiolex/Epidyolex is approved in Israel, Canada, Australia, New Zealand and Taiwan.

Oncology

Rylaze was approved by FDA in June 2021 under the Real-Time Oncology Review program, and was launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with ALL or LBL in pediatric and adult patients one month and older who have developed hypersensitivity to E. coli-derived asparaginase. Rylaze is the only recombinant erwinia asparaginase manufactured product approved in the U.S. that maintains a clinically meaningful level of asparaginase activity throughout the entire course of treatment. We developed Rylaze to address the needs of patients and health care providers for an innovative, high-quality erwinia asparaginase with reliable supply. The initial approved recommended dosage of Rylaze was for an IM administration of 25 mg/m² every 48 hours. In November 2022, FDA approved an sBLA for a Monday/Wednesday/Friday 25/25/50 mg/m² IM dosing schedule. In September 2023, the EC granted marketing authorization for JZP458 under the trade name Enrylaze. This product has also been approved in Great Britain, Canada and Switzerland.

We acquired U.S. development and commercialization rights to Zepzelca in early 2020, and launched six months thereafter, with an indication for treatment of patients with SCLC with disease progression on or after platinum-based chemotherapy. Our education and promotional efforts are focused on SCLC-treating physicians. We are continuing to raise awareness of Zepzelca across academic and community cancer centers. In collaboration with Roche, we have an ongoing Phase 3 pivotal clinical trial of Zepzelca for use as maintenance therapy in first-line extensive-stage SCLC in combination with Tecentriq® (atezolizumab) following induction therapy with carboplatin, etoposide and Tecentriq. In October 2024, we announced positive top-line results from the trial showing a statistically significant and clinically meaningful benefit for Zepzelca and atezolizumab in combination in the first-line maintenance setting. We plan to submit an sNDA in the first half of 2025 to support this combination in the first-line maintenance setting.

We acquired exclusive development and commercialization rights to Ziihera in 2022 through an exclusive licensing agreement with a subsidiary of Zymeworks providing development and commercialization rights to zanidatamab across all indications in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. The term of the license agreement extends on a licensed product-by-licensed product and country-by-country basis until the expiration of the royalty term for such licensed product in such country. We have the right to terminate the amended license agreement at will upon a specified notice period, and either party can terminate the amended license agreement for the other party's uncured material breach or bankruptcy.

Ziihera is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Binding of zanidatamab-hrrii with HER2 results in internalization leading to a reduction of the receptor on the tumor cell surface. In the U.S., Ziihera

was approved by FDA in November 2024 and is indicated for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.

Defitelio is the first and only approved treatment for patients with VOD, sVOD, or VOD with renal or pulmonary dysfunction following HSCT by regulatory authorities in the U.S., Europe, Japan and other markets. Utilization of Defitelio is in part driven by evolving treatment practices in HSCT, and we are continuing to educate healthcare professionals on the clinical profile of Defitelio and its role in treating VOD and/or severe VOD following HSCT.

Vyxeos is a treatment for adults with newly-diagnosed t-AML, or AML-MRC. In March 2021, FDA approved a revised label to include a new indication to treat newly-diagnosed t-AML, or AML-MRC, in pediatric patients aged one year and older. We continue to expand into new markets internationally as the product receives approvals and reimbursement in relevant markets. In the U.S., with ongoing trends towards lower-intensity treatments and away from intensive chemotherapy regimens for AML, we have seen increasing competition from other therapeutic options.

Research and Development Progress

Our research and development activities encompass all stages of development and currently include clinical testing of new product candidates and activities related to clinical improvements of, or additional indications or new clinical data for, our existing marketed products. We also have active preclinical programs for novel therapies, including neuroscience and precision medicines in oncology. We are increasingly leveraging our growing internal research and development function, and we have also entered into collaborations with third parties for the research and development of innovative early-stage product candidates and have supported additional investigator-sponsored trials that are anticipated to generate additional data related to our products. We also seek out investment opportunities in support of the development of early- and mid-stage technologies in our therapeutic areas and adjacencies. We have a number of licensing and collaboration agreements with third parties, including biotechnology companies, academic institutions and research-based companies and institutions, related to preclinical and clinical research and development activities in hematology and in precision oncology, as well as in neuroscience.

Within our oncology R&D program, in October 2022, we announced an exclusive licensing and collaboration agreement with Zymeworks providing us the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the U.S., Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. In December 2022, we exercised the option to continue with the exclusive development and commercialization rights to zanidatamab. Under the terms of the agreement, Zymeworks received an upfront payment of \$50.0 million, and following the exercise of our option to continue the collaboration, a second, one-time payment of \$325.0 million. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to \$1.4 billion, for total potential payments of \$1.76 billion. Zymeworks is eligible to receive tiered royalties between 10% and 20% on our net sales. Zanidatamab is a bispecific HER2-directed antibody that binds to two extracellular sites on HER2. Zanidatamab is currently being evaluated in multiple clinical trials as a treatment for patients with HER2-expressing cancers. Following positive data from a pivotal Phase 2 clinical trial evaluating zanidatamab monotherapy in patients with previously treated advanced or metastatic HER2-amplified BTC, we completed a BLA submission in second-line BTC in March 2024. In May 2024, FDA granted Priority Review of the BLA; we received FDA approval for this BLA in November 2024. EMA has validated our MAA for zanidatamab in second-line BTC; we anticipate a response to our MAA in 2025. In addition, we have an ongoing Phase 3 randomized clinical trial evaluating zanidatamab in combination with chemotherapy plus or minus tislelizumab as a first-line treatment for HER2-expressing GEA, an ongoing Phase 2 trial examining zanidatamab in combination with chemotherapy in first-line patients with HER2-expressing metastatic GEA and an ongoing Phase 3 trial examining zanidatamab in first-line patients with HER2-positive BTC. In July 2024, we announced the initiation of the Phase 3 EmpowHER-BC-303 to evaluate zanidatamab plus chemotherapy or trastuzumab plus chemotherapy in patients with HER2-positive breast cancer whose disease has progressed on previous T-DXd treatment. There are also multiple ongoing clinical trials exploring zanidatamab in breast cancer and other HER2-expressing tumor types.

Our development plan for Zepzelca continues to progress. We are collaborating with Roche on a pivotal Phase 3 clinical trial evaluating Zepzelca in combination with Tecentriq for use as maintenance therapy in first-line extensive-stage SCLC. In October 2024, we announced positive top-line results from the trial showing a statistically significant and clinically meaningful benefit for Zepzelca and atezolizumab in combination in the first-line maintenance setting. We plan to submit an sNDA in the first half of 2025 to support this combination in the first-line maintenance setting. In December 2021, our licensor PharmaMar initiated a confirmatory trial in second-line SCLC. This ongoing three-arm trial is comparing Zepzelca as either monotherapy or in combination with irinotecan to investigator's choice of irinotecan or topotecan. Data from either the first-line trial of Zepzelca in combination with Tecentriq or the PharmaMar trial could serve to confirm clinical benefit of Zepzelca and secure full approval in the U.S.

In addition, we have an ongoing Phase 4 observational study to collect real world safety and outcome data in adult Zepzelca monotherapy patients with SCLC who progress on or after prior platinum-containing chemotherapy. Preliminary findings from this study presented at the 2024 World Conference on Lung Cancer demonstrated Zepzelca provided clinical

benefit when administered as second-line SCLC therapy. The safety and tolerability profile observed in this study was consistent with prior findings, with no new safety signals reported.

In June 2022, we announced FDA had cleared our Investigational New Drug application for JZP815 and, in October 2022, we enrolled the first patient in a Phase 1 trial. JZP815 is an investigational stage pan-RAF kinase inhibitor that targets specific components of the mitogen-activated protein kinase pathway that, when activated by oncogenic mutations, can be a frequent driver of human cancer.

In April 2022, we announced that we had entered into a licensing and collaboration agreement with Werewolf to acquire exclusive global development and commercialization rights to Werewolf's investigational WTX-613, now referred to as JZP898. Under the terms of the agreement, we made an upfront payment of \$15.0 million to Werewolf, and Werewolf is eligible to receive development, regulatory and commercial milestone payments of up to \$1.26 billion. If approved, Werewolf is eligible to receive a tiered, mid-single-digit percentage royalty on net sales of JZP898. This transaction underscores our commitment to enhancing our pipeline to deliver novel oncology therapies to patients, and also provides us with an opportunity to expand into immuno-oncology. JZP898 is a differentiated, conditionally-activated IFN α INDUKINE™ molecule. We initiated a Phase 1 clinical trial of JZP898 in late 2023.

Our neuroscience R&D efforts include an ongoing Phase 3 trial of Epidyolex for LGS, DS and TSC in Japan. In August 2024, we announced top-line results from the trial. The trial did not meet the primary efficacy endpoint of a pre-specified percentage change in indication-associated seizure frequency during the treatment period (up to 16 weeks) compared to baseline in Japanese pediatric patients; however, numeric improvements were observed in the primary and several secondary endpoints. No new safety signals were observed in the trial. We are continuing to collect data in Japanese patients and plan to engage with regulatory authorities in Japan regarding a potential new drug application.

In December 2021, we initiated a Phase 2 clinical trial for suvcaltamide (JZP385), for ET. Additionally, in November 2022, we initiated a Phase 2 trial of suvcaltamide in patients with Parkinson's disease tremor. In June 2024, we announced the ET trial did not achieve statistical significance on the primary and key secondary endpoint for the 30 mg dose. In January 2025, we announced that consistent with the results from the ET trial, results from the Parkinson's disease tremor trial did not show statistical significance on the primary and key secondary endpoint. Based on these results, we will not continue the ET or PDT development program. We are exploring options for the suvcaltamide program. We are also pursuing early-stage activities related to the development of JZP324, an extended-release low sodium, oxybate formulation that we believe could provide a clinically meaningful option for narcolepsy patients.

In May 2022, we announced that we had entered into a licensing agreement with Sumitomo to acquire exclusive development and commercialization rights in the U.S., Europe and other territories for JZP441, also known as DSP-0187, a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. Under the terms of the agreement, we made an upfront payment of \$50.0 million to Sumitomo, and Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to \$1.09 billion. If approved, Sumitomo is eligible to receive a tiered, low double-digit royalty on our net sales of JZP441. In November 2023, we announced that we achieved initial proof-of-concept in our Phase 1 clinical trial program in healthy volunteers as demonstrated by the Maintenance of Wakefulness Test (MWT). At that time, we also noted the program was being paused as we analyzed safety findings related to visual disturbances and cardiovascular effects; no liver toxicity signals were observed. Following additional review of the trial findings and input from FDA, we plan to initiate a small Phase 1b trial of JZP441 in narcolepsy Type 1 patients in 2025. We expect data from this trial will further our understanding of JZP441 and orexin-2 receptor agonism, providing learnings that could inform future development efforts.

Below is a summary of our key ongoing and planned development projects related to our products and pipeline and their corresponding current stages of development:

Product Candidates	Description
ONCOLOGY	
Regulatory	
Zanidatamab	Second-line HER2-expressing BTC (under EMA review)
Phase 3	
Zanidatamab	First-line HER2-positive GEA (ongoing trial)
Zanidatamab	First-line HER2-positive BTC (ongoing trial)
Zanidatamab	Previously treated HER2-positive breast cancer in patients whose disease has progressed on previous T-DXd treatment (EmpowHER-BC-303) (ongoing trial)

Zepzelca	First-line extensive-stage SCLC in combination with Tecentriq (collaboration with Roche) (ongoing trial) Confirmatory second-line trial (PharmaMar study) (ongoing trial)
Výxeos	AML or high-risk MDS (AML18) (cooperative group studies) (ongoing trial) Newly diagnosed adults with standard- and high-risk AML (AML Study Group cooperative group study) (ongoing trial) Newly diagnosed pediatric patients with AML (COG cooperative group study) (ongoing trial)
Phase 2	
Zanidatamab	HER2-expressing GEA, BTC or colorectal cancer in combination with standard first-line chemotherapy (ongoing trial)
Zanidatamab	Basket trial including HER2-positive solid tumors (DiscovHER-Pan-206) (ongoing trial)
Výxeos	High-risk MDS (European Myelodysplastic Syndromes) (cooperative group study) (ongoing trial) Newly diagnosed untreated patients with intermediate- and high-risk AML (cooperative group study) (ongoing trial)
Výxeos + other approved therapies	R/R AML or hypomethylating agent failure MDS (MD Anderson collaboration study) (ongoing trial) De novo or R/R AML (MD Anderson collaboration study) (ongoing trial)
Phase 2a	
Zanidatamab	Previously treated HER2+ HR+ breast cancer in combination with palbociclib (ongoing trial)
Phase 1b/2	
Zanidatamab	First-line breast cancer and GEA (BeiGene trial) (ongoing trial)
Zanidatamab	HER2-expressing breast cancer in combination with ALX148 (ongoing trial)
Phase 1	
JZP815	Raf and Ras mutant tumors (acquired from Redx) (ongoing trial)
Zanidatamab	Previously treated metastatic HER2-expressing cancers in combination with select antineoplastic therapies (cooperative group study) (ongoing trial)
JZP898	Conditionally-activated IFN α INDUKINE™ molecule in solid tumors (ongoing trial)
Výxeos	Low intensity dosing for higher risk MDS (MD Anderson collaboration study) (ongoing trial)
Preclinical	
KRAS inhibitor targets	G12D selective and pan-KRAS molecules (acquired from Redx)
Undisclosed targets	Oncology
CombiPlex®	Hematology/oncology exploratory activities
NEUROSCIENCE	
Phase 3	
Epidyolex	LGS, TSC and DS (ongoing trial in Japan)
Phase 1	
JZP324	Oxybate extended-release formulation (planned trial)
JZP441*	Potent, highly selective oral orexin-2 receptor agonist (ongoing trial)
Preclinical	
Undisclosed targets	Sleep Epilepsy Other Neuroscience

*Also known as DSP-0187

2024 Highlights and Recent Developments

Regulatory Submissions, Approvals and Commercial Launches

- Following positive data from a Phase 2b clinical trial evaluating zanidatamab monotherapy in patients with previously treated advanced or metastatic HER2-amplified BTC, completed a BLA submission in second-line BTC in March 2024. This BLA received Priority Review, and zanidatamab was approved by FDA under the trade name Ziihera in November 2024.
- Launched Ziihera in the U.S. for treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test, in December 2024.
- Based on results from the Phase 2b second-line BTC trial, Ziihera was incorporated into NCCN and ESMO guidelines for BTC treatment.
- Submitted MAA to EMA for zanidatamab in second-line BTC; EMA validated the MAA.
- Reimbursement for Epidyolex was secured in Switzerland, Czech Republic, Estonia, Iceland, Poland and Slovakia for DS, LGS and TSC and in Taiwan for DS and TSC.

Research & Development

- Initiated zanidatamab Phase 3 EmpowHER-BC-303 trial in previously treated HER2-positive breast cancer patients whose disease has progressed on previous T-DXd treatment.
- Initiated zanidatamab Phase 2 DiscovHER-Pan-206 trial to evaluate HER2-positive solid tumors.
- Announced positive top-line findings from the Phase 3 IMforte trial, showing statistically significant and clinically meaningful benefits for Zepzelca and atezolizumab in combination in first-line maintenance therapy for extensive-stage SCLC.
- Reported findings from two Phase 2 trials of suvencaltamide in ET and PDT; these trials did not achieve statistical significance compared to placebo on the primary or key secondary endpoints.
- Reported top-line results from an ongoing Phase 3 trial of Epidyolex for LGS, DS and TSC in Japan. While the trial did not meet the primary efficacy endpoint, numeric improvements were observed in the primary and several secondary endpoints.

Challenges, Risks and Trends Related to Our Business

Our operating plan assumes that Xywav, with 92% lower sodium compared to high-sodium oxybates (depending on the dose) absence of a sodium warning and dosing titration option, will remain the #1 branded oxybate treatment for narcolepsy; the position it held based on revenue in the fourth quarter of 2024. In June 2021, FDA recognized seven years of ODE for Xywav in narcolepsy through July 21, 2027 (which was subsequently extended to January 21, 2028), stating that Xywav is clinically superior to Xyrem by means of greater safety due to reduced chronic sodium burden. While we expect that our business will continue to meaningfully depend on oxybate revenues, there is no guarantee that oxybate revenues will remain at current levels.

Our ability to successfully commercialize Xywav depends on, among other things, our ability to maintain adequate payor coverage and reimbursement for Xywav and acceptance of Xywav by physicians and patients, including of Xywav for the treatment of IH in adults. In an effort to support strong adoption of Xywav and patient success, we are focused on facilitating payor coverage for Xywav and providing robust patient copay and savings programs.

Xywav and Xyrem face competition from a branded product for treatment of cataplexy and/or EDS in narcolepsy. Avadel's Lumryz was launched in the U.S. market in June 2023. On June 22, 2023, we filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA's approval of the NDA for Avadel's Lumryz was unlawful. In the complaint, we alleged that FDA acted outside its authority under the Orphan Drug Act, when, despite ODE protecting Xywav, FDA approved the Lumryz NDA and granted Lumryz ODE based on FDA's finding that Lumryz makes a major contribution to patient care and is therefore clinically superior to Xywav and Xyrem. On September 15, 2023, we filed a motion for summary judgment. On October 20, 2023, Avadel and FDA filed cross motions for summary judgment. Oral argument on these motions was held on May 10, 2024, and on October 30, 2024, the District Court issued an order denying our motion for summary judgment and granting Avadel's and FDA's cross-motions for summary judgment. We have appealed the matter to the United States Court of Appeals for the District of Columbia Circuit. We cannot at this time predict the timing or ultimate outcome of this litigation or the impact of this litigation on our business.

In addition, in January 2023, our oxybate products began to face competition from an AG version of high-sodium oxybate pursuant to a settlement agreement we entered into with an ANDA filer. In July 2023, a volume-limited ANDA filer launched an AG version of high-sodium oxybate. These AG products have negatively impacted and are expected to continue to negatively impact Xyrem and Xywav sales for patients with narcolepsy. Specifically, a wholly owned subsidiary of Hikma launched its AG version of sodium oxybate in January 2023 and Amneal launched its AG version of sodium oxybate in July 2023. Hikma has elected to continue to sell the Hikma AG product, with royalties to be paid to us, for a total of up to four years beginning in January 2024, which election may be terminated by Hikma in accordance with the notice provisions in the agreements between the parties. We have the right to receive a meaningful royalty from Hikma on net sales of the Hikma AG product; the royalty rate was fixed for the second half of 2023. There was a substantial increase in the royalty rate beginning in January 2024, which will remain fixed for the duration of the agreement's term. We are also paid for supply of the Hikma AG product and reimbursed by Hikma for a portion of the services costs associated with the operation of the Xywav and Xyrem REMS, and distribution of the Hikma AG product. We also granted Hikma a license to launch its own generic sodium oxybate product but, if it elects to launch its own generic product, Hikma will no longer have the right to sell the Hikma AG product. In addition, Hikma would need to set up its own REMS (or join an existing REMS operated by another company), which must be open to any other company seeking to commercialize a sodium oxybate product. In our settlements with Amneal, Lupin, and Par, we granted each party the right to sell a limited volume of an AG product in the U.S. beginning on July 1, 2023 and ending on December 31, 2025, with royalties to be paid to us. Amneal launched its AG version of high-sodium oxybate in July 2023. At this time, Amneal has rights to sell a low-single-digit percentage of historical Xyrem sales over each 6-month sales period. At this time, Lupin and Par have elected not to launch an AG product. AG products will be distributed through the same REMS as Xywav and Xyrem. We also granted each of Amneal, Lupin and Par a license to launch its own generic sodium oxybate product under its ANDA on or after December 31, 2025, or earlier under certain circumstances, including the circumstance where Hikma elects to launch its own generic product. If Amneal, Lupin or Par elects to launch its own generic product under such circumstance, it will no longer have the right to sell an AG product. In addition, any company commercializing a generic version of high-sodium oxybate would need to establish its own REMS, or join an existing REMS operated by another company.

In the future, we expect our oxybate products to continue to face competition from generic versions of high-sodium oxybate pursuant to settlement agreements we entered into with multiple ANDA filers. In addition, we received notices in June 2021 and February 2023, that Lupin and Teva, respectively, filed ANDAs for generic versions of Xywav. On October 13, 2023, Lupin announced that it has received tentative approval for its application to market a generic version of Xywav. Generic competition can decrease the net prices at which branded products, such as Xywav and Xyrem are sold, as can competition from other branded products. In addition, we have increasingly experienced pressure from third party payors to agree to discounts, rebates or restrictive pricing terms, and we cannot guarantee we will be able to agree to commercially reasonable terms with PBMs, or similar organizations and other third party payors, or that we will be able to ensure patient access and acceptance on formularies. Entering into agreements with PBMs or similar organizations and payors to ensure patient access has and may continue to result in decreased net prices for some of our products. Moreover, generic or AG high-sodium oxybate products or branded high-sodium oxybate entrants in narcolepsy, such as Avadel's Lumryz, have had and may continue to have the effect of changing payor or formulary coverage of Xywav or Xyrem in favor of other products, and indirectly adversely affect sales of Xywav and Xyrem.

In any event, we expect that the approval and launch of AG products or other generic versions of Xyrem or Xywav and the approval and launch of any other sodium oxybate product, such as Avadel's Lumryz, or alternative product that treats narcolepsy will continue to have a negative impact on, and could have a material adverse effect on, our sales of Xywav and Xyrem and on our business, financial condition, results of operations and growth prospects.

Our financial condition, results of operations and growth prospects are also dependent on our ability to maintain or increase sales of Epidiolex/Epidyolex in the U.S. and Europe, which is subject to many risks and there is no guarantee that we will be able to continue to successfully commercialize Epidiolex/Epidyolex for its approved indications. The commercial success of Epidiolex/Epidyolex depends on the extent to which patients and physicians accept and adopt Epidiolex/Epidyolex as a treatment for seizures associated with LGS, DS and TSC, and we do not know whether our or others' estimates in this regard will be accurate. Physicians may not prescribe Epidiolex and patients may be unwilling to use Epidiolex/Epidyolex if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Additionally, any negative development for Epidiolex/Epidyolex in the market, in clinical development for additional indications, or in regulatory processes in other jurisdictions, may adversely impact the commercial results and potential of Epidiolex/Epidyolex. Moreover, we expect that Epidiolex will face competition from generic products in the future. For example, in November and December 2022, we received notices from ten ANDA filers that they have each filed with FDA an ANDA for a generic version of Epidiolex. In addition, there are non-FDA approved cannabidiol preparations being made available from companies through the state-enabled medical marijuana industry, which might attempt to compete with Epidiolex. Thus, significant uncertainty remains regarding the commercial potential of Epidiolex/Epidyolex.

In addition to our neuroscience products and product candidates, we are commercializing a portfolio of oncology products, including Rylaze, Zepzelca, Ziihera, Defitelio and Vyxeos. An inability to effectively commercialize Rylaze, Zepzelca, Ziihera, Defitelio and Vyxeos and to maximize their potential where possible through successful research and development activities could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

A key aspect of our growth strategy is our continued investment in our evolving and expanding R&D activities. If we are not successful in the clinical development of our product candidates, if we are unable to obtain regulatory approval for our product candidates in a timely manner, or at all, or if sales of an approved product do not reach the levels we expect, our anticipated revenue from our product candidates would be negatively affected, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

In addition to continued investment in our R&D pipeline, we intend to continue to grow our business by acquiring or in-licensing, and developing, including with collaboration partners, additional products and product candidates that we believe are highly differentiated and have significant commercial potential. Failure to identify and acquire, in-license or develop additional products or product candidates, successfully manage the risks associated with integrating any products or product candidates into our portfolio or the risks arising from anticipated and unanticipated problems in connection with an acquisition or in-licensing, such as the GW Acquisition, could have a material adverse effect on our business, results of operations and financial condition.

Our industry has been, and is expected to continue to be, subject to healthcare cost containment and drug pricing scrutiny by regulatory agencies in the U.S. and internationally. If new healthcare policies or reforms intended to curb healthcare costs are adopted or if we experience negative publicity with respect to pricing of our products or the pricing of pharmaceutical drugs generally, the prices that we charge for our products may be affected, our commercial opportunity may be limited and/or our revenues from sales of our products may be negatively impacted. For example, the Inflation Reduction Act of 2022 among other things, requires the U.S. Department of Health and Human Services Secretary to negotiate, with respect to Medicare units and subject to a specified cap, the price of a set number of certain high Medicare spend drugs and biologicals per year starting in 2026, penalizes manufacturers of certain Medicare Parts B and D drugs for price increases above inflation, and makes several changes to the Medicare Part D benefit, including a limit on annual out-of-pocket costs and a change in manufacturer liability under the program, that could negatively affect our business and financial condition. In addition, under the Medicaid Drug Rebate Program, rebates owed by manufacturers are no longer subject to a cap on the rebate amount, which could adversely affect our rebate liability. We are also subject to increasing pricing pressure and restrictions on reimbursement imposed by payors. If we fail to obtain and maintain adequate formulary positions and institutional access for our current products and future approved products, we will not be able to achieve a return on our investment and our business, financial condition, results of operations and growth prospects would be materially adversely affected.

While certain preparations of cannabis remain Schedule I controlled substances, if such products are approved by FDA for medical use in the U.S. they are rescheduled to Schedules II-V, since approval by FDA satisfies the “accepted medical use” requirement; or such products may be removed from control under the Controlled Substances Act entirely. If any of our product candidates receive FDA approval, the Department of Health and Human Services and the U.S. Drug Enforcement Administration will make a scheduling determination. U.S. or foreign regulatory agencies may request additional information regarding the abuse potential of our products which may require us to generate more clinical or other data than we currently anticipate to establish whether or to what extent the substance has an abuse potential, which could increase the cost, delay the approval and/or delay the launch of that product.

Finally, business practices by pharmaceutical companies, including product formulation improvements, patent litigation settlements, and REMS programs, have increasingly drawn public scrutiny from legislators and regulatory agencies, with allegations that such programs are used as a means of improperly blocking or delaying competition. Government investigations with respect to our business practices, including as they relate to the Xywav and Xyrem REMS, the launch of Xywav, our Xyrem patent litigation settlement agreements or otherwise, could cause us to incur significant monetary charges to resolve these matters and could distract us from the operation of our business and execution of our strategy. In addition, from June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with certain generic companies violate state and federal antitrust and consumer protection laws. For additional information on these lawsuits and other legal matters, see Note 13, Commitments and Contingencies-Legal Proceedings of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. It is possible that additional lawsuits will be filed against us making similar or related allegations. We cannot predict the outcome of these or potential additional lawsuits; however, if the plaintiffs were to be successful in their claims against us, they may be entitled to injunctive relief or we may be required to pay significant monetary damages. Moreover, we are, and expect to continue to be, the subject of various claims, legal proceedings, and government investigations apart from those set forth above that have arisen in the ordinary course of business that have not yet been fully resolved and that could

adversely affect our business and the execution of our strategy. Any of the foregoing risks and uncertainties could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Results of Operations

The following table presents our revenues and expenses for the years ended December 31, 2024, 2023 and 2022 (in thousands except percentages):

	2024	Change	2023	Change	2022
Product sales, net	\$ 3,821,164	2 %	\$ 3,736,943	3 %	\$ 3,641,429
Royalties and contract revenues	247,786	155 %	97,261	442 %	17,945
Cost of product sales (excluding amortization of acquired developed technologies)	445,713	2 %	435,577	(19)%	540,517
Selling, general and administrative	1,385,294	3 %	1,343,105	(5)%	1,416,967
Research and development	884,000	4 %	849,658	44 %	590,453
Intangible asset amortization	627,313	3 %	608,284	2 %	599,169
Intangible asset impairment charge	—	— %	—	N/A(1)	133,648
Acquired in-process research and development	10,000	(47)%	19,000	(96)%	444,148
Interest expense, net	238,097	(18)%	289,438	— %	288,242
Foreign exchange (gain) loss	8,182	193 %	(8,787)	(146)%	19,014
Income tax benefit	(91,429)	(24)%	(119,912)	(24)%	(158,645)
Equity in loss of investees	1,660	(45)%	3,009	N/A(1)	9,921

(1) Comparison to prior period is not meaningful.

Revenues

The following table presents product sales, royalties and contract revenues, and total revenues for the years ended December 31, 2024, 2023 and 2022 (in thousands except percentages):

	2024	Change	2023	Change	2022
Xywav	\$ 1,473,202	16 %	\$ 1,272,977	33 %	\$ 958,425
Xyrem	233,816	(59)%	569,730	(44)%	1,020,453
Epidiolex/Epidyolex	972,423	15 %	845,468	15 %	736,398
Sativex	18,877	(4)%	19,668	17 %	16,825
Sunosi ²	—	— %	—	N/A(1)	28,844
Total Neuroscience	2,698,318	— %	2,707,843	(2)%	2,760,945
Rylaze/Enrylaze	410,846	4 %	394,226	40 %	281,659
Zepzelca	320,318	11 %	289,533	7 %	269,912
Defitelio/defibrotide	216,565	18 %	184,000	(5)%	194,290
Vyxeos	162,595	10 %	147,495	15 %	127,980
Ziihera	1,051	N/A(1)	—	— %	—
Total Oncology	1,111,375	9 %	1,015,254	16 %	873,841
Other	11,471	(17)%	13,846	108 %	6,643
Product sales, net	3,821,164	2 %	3,736,943	3 %	3,641,429
High-sodium oxybate AG royalty revenue	217,575	187 %	75,918	N/A(1)	—
Other royalty and contract revenues	30,211	42 %	21,343	19 %	17,945
Total revenues	\$ 4,068,950	6 %	\$ 3,834,204	5 %	\$ 3,659,374

(1) Comparison to prior period is not meaningful.

(2) Net product sales of Sunosi U.S. are included until the date of divestment to Axsome of May 9, 2022.

Product Sales, Net

Xywav product sales increased in 2024 compared to 2023, primarily due to increased sales volumes of 16% and, to a lesser extent, a higher selling price, offset by higher gross to net deductions. We continue to see Xywav adoption in patients

with narcolepsy driven by educational initiatives around efficacy and the benefit of lowering sodium intake. In addition, Xywav product sales were positively impacted by adoption in IH; Xywav is the only oxybate therapy approved to treat IH and we see continued growth of new prescribers. Exiting 2024, there were 10,250 patients taking Xywav for narcolepsy and 3,900 taking Xywav for IH, an increase of approximately 8% and 41%, respectively, compared to 2023. Xywav product sales increased in 2023 compared to 2022, primarily due to increased sales volumes of 28% and, to a lesser extent, a higher selling price. Xyrem product sales decreased in 2024 compared to 2023, primarily due to decreased sales volumes of 57%, due to high-sodium oxybate competition and the adoption of Xywav by existing Xyrem patients and higher gross to net deductions, partially offset by a higher selling price. Xyrem product sales decreased in 2023 compared to 2022, primarily due to decreased sales volumes of 49%, reflecting the adoption of Xywav by existing Xyrem patients and the impact of high-sodium oxybate competition, offset by a higher selling price and lower gross to net deductions. Epidiolex/Epidyolox product sales increased by 15% in 2024 compared to 2023, primarily due to increased sales volumes of 12% due to increased demand, and, to a lesser extent, geographic expansion and a higher average selling price. Epidiolex/Epidyolox product sales increased by 15% in 2023 compared to 2022, primarily due to increased sales volumes of 15% due to increased demand and expansion in European markets and, to a lesser extent, a higher average selling price, partially offset by higher gross to net deductions.

Rylaze/Enrylaze product sales increased in 2024 compared to 2023, primarily due to a higher average selling price, partially offset by higher gross to net deductions. Rylaze sales volumes in 2024 have been negatively impacted due to an update to the COG pediatric treatment protocols for ALL, which impacts the timing of asparaginase administration. While this had a temporary negative impact on Rylaze product sales in the latter part of 2024, we do not expect it will affect ongoing demand and we still expect our product sales to normalize by early 2025. Rylaze remains the only therapy available to patients in the U.S. who have a hypersensitivity reaction to E. coli-derived asparaginase. Rylaze product sales increased in 2023 compared to 2022, primarily due to increased sales volumes of 37% and, to a lesser extent, a higher selling price, offset by higher gross to net deductions. The increased sales volumes reflected the significant unmet patient need for a high-quality, reliable supply of Erwinia asparaginase for patients with ALL. Zepzelca product sales increased by 11% in 2024 compared to 2023, primarily due to increased sales volumes and a higher selling price, offset by higher gross to net deductions. Zepzelca product sales increased by 7% in 2023 compared to 2022, primarily due to a higher selling price and increased sales volumes, offset by higher gross to net deductions. Defitelio/defibrotide product sales decreased by 5% in 2023 compared to 2022, primarily due to a decrease in sales volumes, partially offset by a higher selling price. Vyxeos product sales increased by 10% in 2024 compared to 2023, primarily due to increased sales volumes, partially offset by a lower average selling price due to regional mix. Vyxeos product sales increased by 15% in 2023 compared to 2022, primarily due to increased sales volumes and to a lesser extent, a higher selling price, partially offset by higher gross to net deductions.

We expect product sales, net will increase in 2025 over 2024, primarily driven by growth across our commercial portfolio, offset by a decrease in sales of Xyrem due to the impact of high-sodium oxybate competition.

Royalties and Contract Revenues

Royalties and contract revenues increased in 2024 compared to 2023 and in 2023 compared to 2022 primarily due to royalty revenue received from Hikma on net sales of their high-sodium oxybate AG. We expect royalties and contract revenues to increase in 2025 compared to 2024, primarily due to increased royalty revenues arising from net sales of high-sodium oxybate AG.

Cost of Product Sales

Cost of product sales increased in 2024 compared to 2023, due to increased inventory provisions and changes in product mix, offset by a decrease in the fair value step-up expense, of \$16.4 million. Cost of product sales decreased in 2023 compared to 2022, primarily due to a reduction in the fair value step-up expense of \$121.9 million and the impact of an expense for past royalties recorded in 2022 in connection with a settlement agreement with Otsuka, partially offset by changes in product mix. Gross margin as a percentage of net product sales was 88.3% in both 2024 and 2023 and 85.2% in 2022. The increase in our gross margin percentage in 2023 compared to 2022 was primarily due to the decrease in the fair value step-up expense in 2023 and the impact of the Otsuka royalty expense in 2022.

We expect our cost of product sales to increase in 2025 compared to 2024, primarily driven by changes in product mix.

Selling, General and Administrative Expenses

Selling, general and administrative expenses increased in 2024 compared to 2023, primarily due to increased compensation-related expenses of \$72.6 million, primarily driven by higher headcount and increased investment in sales and marketing of \$19.3 million, in support of our commercial portfolio and increased litigation costs of \$13.6 million, partially offset by costs relating to the impairment of facility assets of \$61.7 million and program terminations of \$23.5 million incurred in 2023. Selling, general and administrative expenses decreased in 2023 compared to 2022, primarily due to the loss on

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disposal of Sunosi of \$40.8 million, restructuring costs of \$22.1 million and GW related integration costs of \$21.1 million incurred in 2022, together with a reduction in costs related to program terminations of \$19.1 million and in compensation related expenses, partially offset by an impairment of facility assets of \$61.7 million in 2023. We expect selling, general and administrative expenses in 2025 to increase compared to 2024, primarily due to investment in our commercial portfolio, including the launch of Zihera, along with increased compensation-related expenses.

Research and Development Expenses

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses, milestone expenses and other research and development costs. Clinical study and outside services costs relate primarily to services performed by clinical research organizations, materials and supplies, and other third party fees. Personnel expenses relate primarily to salaries, benefits and share-based compensation. Other research and development expenses primarily include overhead allocations consisting of various support and facilities-related costs. We do not track fully-burdened research and development expenses on a project-by-project basis. We manage our research and development expenses by identifying the research and development activities that we anticipate will be performed during a given period and then prioritizing efforts based on our assessment of which development activities are important to our business and have a reasonable probability of success, and by dynamically allocating resources accordingly. We also continually review our development pipeline projects and the status of their development and, as necessary, reallocate resources among our development pipeline projects that we believe will best support the future growth of our business.

The following table provides a breakout of our research and development expenses by major categories of expense (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Clinical studies and outside services	\$ 510,941	\$ 501,181	\$ 270,008
Personnel expenses	290,856	258,303	223,603
Milestone expense	2,500	5,500	6,250
Restructuring expenses	—	—	10,284
Other	79,703	84,674	80,308
Total	<u>\$ 884,000</u>	<u>\$ 849,658</u>	<u>\$ 590,453</u>

Research and development expenses increased by \$34.3 million in 2024 compared to 2023. Clinical studies and outside services costs increased in 2024 compared to 2023, primarily due to the addition of costs related to clinical programs for zanidatamab, partially offset by a reduction in costs related to JZP150 (post-traumatic stress disorder) and JZP385. Personnel expenses increased by \$32.6 million in 2024 compared to 2023, primarily due to increased compensation related expenses in support of our development programs. Research and development expenses increased by \$259.2 million in 2023 compared to 2022. Clinical studies and outside services costs increased in 2023 compared to 2022, primarily due to the addition of costs related to clinical programs for zanidatamab, and, to a lesser extent, JZP385 and JZP441, partially offset by a reduction in costs related to JZP458 (Rylaze). Personnel expenses increased by \$34.7 million in 2023 compared to 2022, primarily due to increased headcount in support of our development programs. Milestone expenses of \$5.5 million in 2023 primarily related to a milestone expense of \$5.0 million under our collaboration and license agreement with Werewolf. Milestone expenses of \$6.3 million in 2022 primarily related to a milestone expense of \$5.0 million made under our asset purchase and collaboration agreements with Redx. We incurred restructuring costs of \$10.3 million in 2022.

For 2025, we expect that our research and development expenses will decrease compared to 2024, primarily driven by a reduction in clinical studies and outside services costs relating to JZP385 and continued portfolio prioritization.

Intangible Asset Amortization

Intangible asset amortization increased by \$19.0 million in 2024 compared to 2023, primarily due to the foreign exchange impact on our sterling-denominated intangible assets. Intangible asset amortization for 2023 was in line with 2022. Intangible asset amortization in 2025 is expected to be broadly in line with 2024.

Acquired In-Process Research and Development

Acquired IPR&D expense in 2024 related to the upfront payment made in connection with our asset purchase agreement with Redx, of \$10.0 million. Acquired IPR&D expense in 2023 primarily related to the upfront payment made in connection with our licensing and collaboration agreement with Autifony of \$18.0 million. Acquired IPR&D expense in 2022 primarily related to the upfront payments made in connection with our licensing and collaboration agreements with Zymeworks and Werewolf of \$375.0 million and \$15.0 million, respectively, and our licensing agreement with Sumitomo of \$50.0 million.

Intangible Asset Impairment Charge

In 2022, we recorded an acquired IPR&D asset impairment charge of \$133.6 million as a result of the decision to discontinue our nabiximols program.

Interest Expense, Net

Interest expense, net decreased by \$51.3 million in 2024 compared to 2023, primarily due to higher interest income on investments driven by our increased deposits and higher interest rates and lower interest expense on the Tranche B-2 Dollar Term Loans following the 2024 repricings described under “Liquidity and Capital Resources—Credit Agreement” below, offset by the inclusion of interest expense on our 2030 Notes. Interest expense, net increased by \$1.2 million in 2023 compared to 2022, primarily driven by higher interest rates on our outstanding term loan borrowings, partially offset by higher interest income on investments and the inclusion of interest expense on the now repaid Euro Term Loan, in 2022.

We expect interest expense, net to decrease in 2025 compared to 2024 primarily due to lower interest expense following the voluntary repayment of \$750.0 million on our Tranche B-2 Dollar Term Loans in January 2025, partially offset by lower interest income and interest expense on the 2030 Notes. For further information on this please refer to Liquidity and Capital Resources.

Foreign Exchange (Gain) Loss

The foreign exchange (gain) loss is primarily related to the translation of sterling and euro-denominated net monetary liabilities, primarily intercompany balances, held by subsidiaries with a U.S. dollar functional currency and related foreign exchange forward contracts not designated as hedging instruments.

Income Tax Benefit

Our income tax benefit was \$91.4 million, \$119.9 million and \$158.6 million in 2024, 2023 and 2022, respectively, relating to tax arising on income or losses in Ireland, the U.K., the U.S. and certain other foreign jurisdictions, offset by deductions on subsidiary equity, patent box benefits, foreign derived intangible income benefits and originating tax credits. Our income tax benefit in 2024 decreased compared to 2023 primarily due to the change in income mix across jurisdictions, partially offset by patent box benefits. Our income tax benefit in 2023 decreased compared to 2022 primarily due to pretax losses from payments for acquired IPR&D made in 2022 and the impact of the 2022 impairment of our acquired IPR&D asset as a result of the decision to discontinue our nabiximols program, partially offset by the change in income mix across jurisdictions.

Equity in Loss of Investees

Equity in loss of investees relates to our share in the net loss of companies in which we have made investments accounted for under the equity method of accounting.

Liquidity and Capital Resources

As of December 31, 2024, we had cash, cash equivalents and investments of \$3.0 billion, borrowing available under our Amended Revolving Credit Facility of \$885.0 million and a long-term debt principal balance of \$6.2 billion. Our long-term debt included \$2.7 billion aggregate principal amount of the Tranche B-2 Dollar Term Loans, \$1.5 billion in aggregate principal amount of the Secured Notes, \$1.0 billion principal amount of the 2026 Notes and \$1.0 billion principal amount of the 2030 Notes. During 2024, 2023 and 2022, we generated cash flows from operations of \$1.4 billion, \$1.1 billion and \$1.3 billion, respectively, and we expect to continue to generate positive cash flow from operations which we expect will enable us to operate our business and de-lever our balance sheet over time.

Since the closing of the acquisition of GW in May 2021, we have fully repaid our Euro Term Loan. With respect to our Tranche B-2 Dollar Term Loans, we have made voluntary repayments of \$1.1 billion, \$300.0 million in September 2022 and \$750.0 million in January 2025, along with mandatory repayments of \$108.5 million. In August 2024, we repaid the \$575.0 million aggregate principal amount of our 2024 Notes.

We have a significant amount of debt outstanding on a consolidated basis. For a more detailed description of our debt arrangements, including information relating to our scheduled maturities with respect to our long-term debt see Note 11, Debt, of the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. This substantial level of debt could have important consequences to our business, including, but not limited to the factors set forth in in Part I, Item 1A “Risk Factors” of this Annual Report on Form 10-K under the heading “We have incurred substantial debt, which could impair our flexibility and access to capital and adversely affect our financial position, and our business would be adversely affected if we are unable to service our debt obligations.”

We believe that our existing cash, cash equivalents and investments balances, cash we expect to generate from operations and funds available under our Amended Revolving Credit Facility will be sufficient to fund our operations and to meet our

existing obligations for the foreseeable future. The adequacy of our cash resources depends on many assumptions, including primarily our assumptions with respect to product sales and expenses, as well as the other factors set forth in “Risk Factors” in Part I, Item 1A of this Annual Report on Form 10-K under the headings “Risks Related to our Lead Products and Product Candidates” and *“To continue to grow our business, we will need to commit substantial resources, which could result in future losses or otherwise limit our opportunities or affect our ability to operate and grow our business.”* Our assumptions may prove to be wrong or other factors may adversely affect our business, and as a result we could exhaust or significantly decrease our available cash resources, and we may not be able to generate sufficient cash to service our debt obligations which could, among other things, force us to raise additional funds and/or force us to reduce our expenses, either of which could have a material adverse effect on our business.

To continue to grow our business over the longer term, we plan to commit substantial resources to product acquisition and in-licensing, product development, clinical trials of product candidates and expansion of our commercial, development, manufacturing and other operations. In this regard, we have evaluated and expect to continue to evaluate a wide array of strategic transactions as part of our strategy to acquire or in-license and develop additional products and product candidates. Acquisition opportunities that we pursue could materially affect our liquidity and capital resources and may require us to incur additional indebtedness, seek equity capital or both. We regularly evaluate the performance of our products and product candidates to ensure fit within our portfolio and support efficient allocation of capital. In addition, we may pursue new operations or continue the expansion of our existing operations. Accordingly, we expect to continue to opportunistically seek access to additional capital to license or acquire additional products, product candidates or companies to expand our operations or for general corporate purposes. Raising additional capital could be accomplished through one or more public or private debt or equity financings, collaborations or partnering arrangements. However, our ability to raise additional capital may be adversely impacted by worsening global economic conditions and the recent disruptions to, and volatility in, the credit and financial markets in the U.S. and worldwide resulting from the effects of inflationary pressures, potential future bank failures, or otherwise. Accordingly, we could experience an inability to access additional capital or our liquidity could otherwise be impacted, which could in the future negatively affect our capacity for certain corporate development transactions or our ability to make other important, opportunistic investments. In addition, under Irish law we must have authority from our shareholders to issue any ordinary shares, including ordinary shares that are part of our authorized but unissued share capital, and we currently have such authorization. Moreover, as a matter of Irish law, when an Irish public limited company issues ordinary shares to new shareholders for cash, the company must first offer those shares on the same or more favorable terms to existing shareholders on a pro rata basis, unless this statutory pre-emption obligation is dis-applied, or opted-out of, by approval of its shareholders. At our annual general meeting of shareholders in July 2024, our shareholders voted to approve our proposal to dis-apply the statutory pre-emption obligation. This current pre-emption opt-out authority is due to expire in January 2026. If we are unable to obtain further pre-emption authorities from our shareholders in the future, or otherwise continue to be limited by the terms of new pre-emption authorities approved by our shareholders in the future, our ability to use our unissued share capital to fund in-licensing, acquisition or other business opportunities, or to otherwise raise capital, including at the time we are required to make repurchases of the 2026 Notes, the 2030 Notes and/or the Secured Notes, are required to repay outstanding amounts under the Amended Credit Agreement, or pay cash upon exchange of the 2026 Notes or the 2030 Notes, could likewise be adversely affected. In any event, an inability to borrow or raise additional capital in a timely manner and on attractive terms could prevent us from expanding our business or taking advantage of acquisition opportunities and could otherwise have a material adverse effect on our business and growth prospects. In addition, if we use a substantial amount of our funds to acquire or in-license products or product candidates, we may not have sufficient additional funds to conduct all of our operations in the manner we would otherwise choose. Furthermore, any equity financing would be dilutive to our shareholders, and could require the consent of the lenders under the Amended Credit Agreement that provides for (i) the Tranche B-2 Dollar Term Loans and Amended Revolving Credit Facility, and the indenture for the Secured Notes for certain financings.

In July 2024, our board of directors authorized the New Repurchase Program. Under the New Repurchase Program, which has no expiration date, we may repurchase ordinary shares from time to time by any methods and/or structures permitted by applicable law. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the Amended Credit Agreement and the indenture for our Secured Notes, corporate and regulatory requirements and market conditions. The New Repurchase Program may be modified, suspended or discontinued at any time without our prior notice. The New Repurchase Program replaces and supersedes the Old Repurchase Program. In 2024, we spent a total of \$311.4 million to purchase 2.8 million of our ordinary shares under the repurchase programs at an average total purchase price, including commissions, of \$110.06 per share. The repurchases in 2024 included a total of \$150.0 million to repurchase 1.4 million of our ordinary shares, all under the New Repurchase Program, at a purchase price, including commissions, of \$109.32 per share and \$161.4 million to repurchase 1.5 million of our ordinary shares, all under the Old Repurchase Program, at a purchase price, including commissions, of \$110.75 per share. The repurchases made under the New Repurchase Program in 2024 were effected in privately negotiated transactions with or through one of the initial purchasers of the 2030 Notes concurrently with the pricing of the offering of the 2030 Notes. In 2023, we spent a total of \$269.8 million to purchase 2.1 million of our ordinary shares under the Old Repurchase Program at an average total purchase price, including commissions, of \$126.65 per share. All ordinary shares repurchased were cancelled. As of December 31, 2024, the remaining amount authorized for repurchases under the New Repurchase Program was \$350.0 million, exclusive of any brokerage commissions.

The following table shows a summary of our cash flows for the periods indicated (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Net cash provided by operating activities	\$ 1,395,908	\$ 1,092,007	\$ 1,271,977
Net cash used in investing activities	(508,195)	(163,062)	(446,230)
Net cash provided by (used in) financing activities	20,516	(305,254)	(529,491)
Effect of exchange rates on cash and cash equivalents	(1,675)	1,137	(6,222)
Net increase in cash and cash equivalents	<u>\$ 906,554</u>	<u>\$ 624,828</u>	<u>\$ 290,034</u>

Operating activities

Net cash provided by operating activities increased by \$303.9 million in 2024 compared to 2023, primarily due to cash received from increased sales of our products, decreased prepaid income taxes and the timing of payment of accrued expenses.

Net cash provided by operating activities decreased by \$180.0 million in 2023 compared to 2022, primarily due to an increase in research and development expenses primarily related to zanidatamab, increased prepaid income taxes and increased interest expense on our outstanding term loan borrowings.

Investing activities

Net cash used in investing activities increased by \$345.1 million in 2024 compared to 2023, primarily due to the following:

- \$340.0 million net increase in the acquisition of investments, driven by time deposits; and
- \$14.1 million increase in purchases of property, plant and equipment; offset by
- \$9.0 million decrease in upfront payments for acquired IPR&D driven by the \$18.0 million payment to Autifony in 2023, partially offset by the \$10.0 million payment to Redx in 2024.

Net cash used in investing activities decreased by \$283.2 million in 2023 compared to 2022, primarily due to the following:

- \$425.1 million decrease in upfront payments for acquired IPR&D primarily driven by the \$375.0 million, \$50.0 million and \$15.0 million payments to Zymeworks, Sumitomo and Werewolf, respectively, in 2022, partially offset by the \$18.0 million payment to Autifony in 2023; offset by
- \$119.1 million net increase in the acquisition of investments, primarily time deposits; and
- \$53.0 million upfront payment from Axxome in 2022 relating to the Sunosi U.S. disposition.

Financing activities

Net cash provided by (used in) financing activities increased by \$325.8 million in 2024 compared to 2023, primarily due to:

- An increase of \$405.8 million in debt financing due to net proceeds from issuance of the 2030 Notes of \$980.8 million, offset by the repayment of the 2024 Notes of \$575.0 million; partially offset by
- An increase of \$41.7 million in share repurchases; and
- A decrease of \$25.8 million in proceeds from employee equity incentive and purchase plans.

Net cash used in financing activities decreased by \$224.2 million in 2023 compared to 2022, primarily due to:

- Repayments of long-term debt of \$31.0 million in 2023, compared to \$582.0 million in 2022; offset by
- Share repurchases of \$269.8 million in 2023; and
- A decrease of \$51.6 million in proceeds from employee equity incentive and purchase plans.

Credit Agreement

On May 5, 2021, Jazz Pharmaceuticals plc, Jazz Lux, and certain of our other subsidiaries, as borrowers, or, collectively with Jazz Pharmaceuticals plc and Jazz Lux, the “Borrowers”, entered into the Credit Agreement. The Credit Agreement initially provided for (i) the Dollar Term Loan, which was drawn by Jazz Lux on the closing date thereof in U.S. dollars (ii) the Euro Term Loan, which was drawn by Jazz Lux on the closing date thereof in Euros and (iii) the Initial Revolving Credit Facility.

In January 2024, Jazz Lux entered into the Repricing Amendment No.1, to the Credit Agreement. Upon entry into the Repricing Amendment No.1, certain existing lenders converted a portion of the outstanding Dollar Term Loan into the Tranche B-1 Dollar Term Loans, and Jazz Lux borrowed \$201.9 million aggregate principal amount of additional Tranche B-1 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Dollar Term Loan that was not converted.

In July 2024, Jazz Lux entered into the Repricing Amendment No. 2, to the Credit Agreement, as amended by the Repricing Amendment No. 1. Upon entry into the Repricing Amendment No. 2, certain existing lenders converted a portion of the outstanding Tranche B-1 Dollar Term Loans into the Tranche B-2 Dollar Term Loans, and Jazz Lux borrowed \$289.6 million aggregate principal amount of additional Tranche B-2 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Tranche B-1 Dollar Term Loans that were not converted.

The Tranche B-2 Dollar Term Loans are a separate class of term loans under the Credit Agreement, as amended by Repricing Amendment No. 1 and Repricing Amendment No. 2, with the same material terms (including with respect to maturity, prepayment, security, covenants and events of default) as the previously outstanding Tranche B-1 Dollar Term Loans and the initial Dollar Term Loan incurred on May 5, 2021, with the interest rate amended as described below and the credit spread adjustment removed. The principal amount of Tranche B-1 Dollar Term Loans outstanding immediately prior to the Repricing Amendment No. 2 and the outstanding principal amount of Tranche B-2 Dollar Term Loans immediately following the Repricing Amendment No.2, each totaled \$2.7 billion.

The Tranche B-2 Dollar Term Loans bear interest at a rate equal to either (a) Term SOFR, or (b) the prime lending rate, in each case, plus an applicable margin. The applicable margin for the Tranche B-2 Dollar Term Loans is 2.25% (in the case of Term SOFR borrowings) and 1.25% (in the case of borrowings at the prime lending rate), a decrease, in each case, of 75 basis points from the applicable margin on the Tranche B-1 Dollar Term Loans. The Tranche B-2 Dollar Term Loans are subject to a Term SOFR floor of 0.50%. As of December 31, 2024, the interest rate and effective interest rate on the Tranche B-2 Dollar Term Loans were 6.61% and 8.27%, respectively.

In November 2024, we entered into Amendment No. 3 to the Credit Agreement, as amended by the Repricing Amendment No. 1 and Repricing Amendment No. 2, to increase the Initial Revolving Credit Facility from \$500.0 million to \$885.0 million and extend the maturity date from May 5, 2026 to the Amended Revolving Facility Maturity Date, provided that:

- if, as of any date from March 16, 2026 to the 2026 Notes Springing Maturity Date, (x) any 2026 Maturity Indebtedness remains outstanding and (y) the aggregate amount of unrestricted cash of Jazz Pharmaceuticals plc and its subsidiaries is less than an amount equal to 125% of the aggregate principal amount of 2026 Maturity Indebtedness outstanding, then the maturity date for the Amended Revolving Credit Facility will be shortened to the 2026 Notes Springing Maturity Date;
- if, as of February 4, 2028, (x) more than \$500,000,000 of the Term Loan Indebtedness remains outstanding and (y) the maturity date of such Term Loan Indebtedness is not later than the date that is 91 days after the Amended

Revolving Facility Maturity Date, then the maturity date for the Amended Revolving Credit Facility will be shortened to February 4, 2028; and

- if, as of the Senior Notes Springing Maturity Date, (x) more than \$500,000,000 of the Senior Note Indebtedness remains outstanding and (y) the maturity date with respect to such Senior Note Indebtedness is not later than the date that is 91 days after the Amended Revolving Facility Maturity Date, then the maturity date for the Amended Revolving Credit Facility will be shortened to October 16, 2028.

Initially, the applicable margin for the loans under the Amended Revolving Credit Facility will be 2.00% (in the case of Term SOFR borrowings) and 1.00% (in the case of borrowings at the prime lending rate).

Thereafter, the applicable margin for the Amended Revolving Credit Facility ranges from 1.75% to 2.75% (in the case of Term SOFR borrowings) and 0.75% to 1.75% (in the case of borrowings at the prime lending rate), depending on our first lien secured net leverage ratio level, and any loans under the Amended Revolving Credit Facility are subject to a Term SOFR floor of 0.00%. The Amended Revolving Credit Facility has a commitment fee payable on the undrawn amount ranging from 0.25% to 0.45% per annum based upon our first lien secured net leverage ratio. As of December 31, 2024, we had an undrawn Amended Revolving Credit Facility totaling \$885.0 million.

2029 Senior Secured Notes

On April 29, 2021, Jazz Securities, a wholly owned subsidiary of Jazz Pharmaceuticals plc, closed the offering of the Secured Notes in a private placement. We used the proceeds from the Secured Notes to fund, in part, the cash consideration payable in connection with the GW Acquisition.

Interest on the Secured Notes is payable semi-annually in arrears on January 15 and July 15 of each year, beginning on January 15, 2022, at a rate of 4.375% per year. The Secured Notes mature on January 15, 2029.

The Secured Notes are jointly and severally guaranteed by us and each of our restricted subsidiaries, other than Jazz Securities, that is a borrower, or a guarantor, under the Amended Credit Agreement. The Secured Notes and related guarantees are secured by a first priority lien (subject to permitted liens and certain other exceptions), equally and ratably with the Amended Credit Agreement, on the collateral securing the Amended Credit Agreement.

Some or all of the Secured Notes, may be redeemed at any time and from time to time at a specified redemption prices, plus accrued and unpaid interest, if any, to, but excluding, to the redemption date. In addition, Jazz Securities may redeem all but not part of the Secured Notes at its option at any time in connection with certain tax-related events at a price equal to 100% of the principal amount of the Secured Notes to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date.

If we undergo a change of control, Jazz Securities will be required to make an offer to purchase all of the Secured Notes at a purchase price in cash equal to 101% of the principal amount thereof, plus accrued and unpaid interest, if any, to, but excluding, the date of repurchase, subject to certain exceptions.

The indenture governing the Secured Notes contains customary affirmative covenants and negative covenants applicable to us and our restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. If Jazz Securities or our restricted subsidiaries engage in certain asset sales, Jazz Securities will be required under certain circumstances to make an offer to purchase the Secured Notes at 100% of the principal amount, plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.

As of December 31, 2024, the interest rate and effective interest rate on the Secured Notes were 4.375% and 4.64%, respectively.

Exchangeable Senior Notes

2030 Notes. In September 2024, Jazz Investments, our wholly owned subsidiary, completed a private placement of \$1.0 billion principal amount of the 2030 Notes.

Interest on the 2030 Notes is payable semi-annually in cash in arrears on March 15 and September 15 of each year, beginning on March 15, 2025, at a rate of 3.125% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2030 Notes. The 2030 Notes mature on September 15, 2030, unless earlier exchanged, redeemed or repurchased.

The holders of the 2030 Notes have the ability to require us to repurchase all or a portion of their 2030 Notes for cash at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date in the event we undergo a fundamental change (as defined in the indenture related to the 2030 Notes), such as specified change of control transactions, our liquidation or

dissolution or the delisting of our ordinary shares from any of The New York Stock Exchange, The Nasdaq Global Market, The Nasdaq Global Select Market or The Nasdaq Capital Market (or any of their respective successors).

Additionally, the terms and covenants in the indenture related to the 2030 Notes include certain events of default after which the 2030 Notes may be due and payable immediately.

Prior to September 15, 2030, we may redeem the 2030 Notes, in whole but not in part, in connection with certain tax-related events. We also may redeem the 2030 Notes on or after September 20, 2027 and prior to June 15, 2030, in whole or in part (subject to the partial redemption limitation described in the indenture related to the 2030 Notes), if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

The 2030 Notes are exchangeable at an initial exchange rate of 6.5339 ordinary shares per \$1,000 principal amount of 2030 Notes, which is equivalent to an initial exchange price of approximately \$153.05 per ordinary share. Upon exchange of the 2030 Notes, we will pay cash up to the aggregate principal amount of the 2030 Notes to be exchanged and pay or deliver, as the case may be, cash, ordinary shares or a combination of cash and ordinary shares, at our election, in respect of the remainder, if any, of our exchange obligation in excess of the aggregate principal amount of the 2030 Notes being exchanged. The exchange rate is subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes (as defined in the indenture related to the 2030 Notes) that occur prior to the maturity date or upon our issuance of a notice of redemption, we will, in certain circumstances, increase the exchange rate for a holder who elects to exchange its 2030 Notes in connection with that make-whole fundamental change or exchange its 2030 Notes called (or deemed called) for redemption during the related redemption period. Prior to June 15, 2030, the 2030 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

2026 Notes. In June 2020, Jazz Investments completed a private placement of \$1.0 billion principal amount of the 2026 Notes. We used a portion of the net proceeds from this offering to repurchase for cash \$332.9 million aggregate principal amount of the 1.875% exchangeable senior notes due 2021, through privately-negotiated transactions concurrently with the offering of the 2026 Notes. Interest on the 2026 Notes is payable semi-annually in cash in arrears on June 15 and December 15 of each year, beginning on December 15, 2020, at a rate of 2.00% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2026 Notes. The 2026 Notes mature on June 15, 2026, unless earlier exchanged, repurchased or redeemed.

The holders of the 2026 Notes have the ability to require us to repurchase all or a portion of their 2026 Notes for cash in the event we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from any of The New York Stock Exchange, The Nasdaq Global Market, The Nasdaq Global Select Market or The Nasdaq Capital Market (or any of their respective successors). Additionally, the terms and covenants in the indenture related to the 2026 Notes include certain events of default after which the 2026 Notes may be due and payable immediately. Prior to June 15, 2026, we may redeem the 2026 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2026 Notes additional amounts as a result of certain tax-related events. We also may redeem the 2026 Notes prior to March 15, 2026, in whole or in part, if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide the notice of redemption.

The 2026 Notes are exchangeable at an initial exchange rate of 6.4182 ordinary shares per \$1,000 principal amount of 2026 Notes, which is equivalent to an initial exchange price of approximately \$155.81 per ordinary share. On July 22, 2024, we irrevocably elected to fix the settlement method for exchange of the 2026 Notes to a combination of cash and ordinary shares of Jazz Pharmaceuticals plc with a specified cash amount per \$1,000 principal amount of 2026 Notes exchanged equal to or in excess of \$1,000. As a result, for any 2026 Notes exchanged subsequent to such notice, an exchanging holder will receive (i) up to \$1,000 in cash per \$1,000 principal amount of 2026 Notes exchanged and (ii) cash, ordinary shares, or any combination thereof, at our election, in respect of the remainder, if any, of its exchange obligation in excess of \$1,000 per \$1,000 principal amount of 2026 Notes exchanged. The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes occurring prior to the maturity date of the 2026 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2026 Notes who elect to exchange their 2026 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to March 15, 2026, the 2026 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

2024 Notes. In 2017, Jazz Investments completed a private placement of \$575.0 million principal amount of 2024 Notes. We used the net proceeds from this offering to repay \$500.0 million in outstanding loans under the Initial Revolving Credit Facility and to pay related fees and expenses. We used the remainder of the net proceeds for general corporate purposes. Interest on the 2024 Notes was payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2018, at a rate of 1.50% per year. The 2024 Notes were exchangeable at an initial exchange rate of 4.5659 ordinary shares per \$1,000 principal amount of 2024 Notes, which was equivalent to an initial exchange price of approximately \$219.02 per ordinary share.

On August 15, 2024, the maturity date for the 2024 Notes, we repaid the \$575.0 million aggregate principal amount, plus accrued and unpaid interest thereon.

Contractual Obligations

Our primary contractual obligations relate to our outstanding indebtedness, as described above. We also have obligations under lease agreements and third-party manufacturing agreements. For information relating to our scheduled maturities with respect to our long-term debt and our lease liabilities see Note 11 Debt and Note 12 Leases, respectively, and for information relating to our noncancelable purchase commitments due within one year see Note 13 Commitments and Contingencies, included in the Notes to Consolidated Financial Statements, included in Part IV of this Annual Report on Form 10-K. Our long-term noncancelable purchase commitments were \$31.7 million at December 31, 2024, primarily related to agreements with third party manufactures.

We also have potential future milestone payments or royalty obligations to third parties under asset purchase, product development, license and other agreements as the timing and likelihood of such milestone payments are not known, and, in the case of royalty obligations, as the amount of such obligations are not estimable. Our contingent obligations to third parties, in the form of development, regulatory and sales-based milestone payments, as of December 31, 2024 included \$1,362.5 million under our license and collaboration agreement with Zymeworks, \$1,255.0 million under our global license and collaboration agreement with Werewolf, \$1,090.0 million under our license agreement with Sumitomo, \$1,065.0 million under our asset purchase agreements with Redx, \$752.5 million under our license and collaboration agreement with Autifony, \$581.0 million under our amended license agreement with PharmaMar, \$375.0 million under the asset purchase and exclusive license agreement with SpringWorks Therapeutics, Inc., \$260.0 million in connection with our acquisition of Cavion, \$155.5 million under our license agreement with Ligand, and \$492.4 million related to other agreements.

Critical Accounting Policies and Significant Estimates

A critical accounting policy is one that is both important to the portrayal of our financial condition and results of operations and requires management's most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. While our significant accounting policies are described in more detail in Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K, we believe the following accounting estimates and policies to be critical.

Revenue Recognition

Revenues are recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services.

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

Items Deducted from Gross Product Sales.

Revenues from sales of products are recorded net of government rebates and rebates under managed care plans and commercial payor contracts, estimated allowances for sales returns, government chargebacks, prompt payment discounts, patient coupon programs, and specialty distributor and wholesaler fees. Calculating certain of these items involves estimates and judgments based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in applicable regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data. We review the adequacy of our provisions for sales deductions on a quarterly basis. Amounts accrued for sales deductions are adjusted when trends or significant events indicate that adjustment is appropriate and to reflect actual experience. The most significant items deducted from gross product sales where we exercise judgment are rebates, sales returns and chargebacks.

The following table presents the activity and ending balances for our sales-related accruals and allowances (in thousands):

	Rebates Payable	Sales Returns Reserve	Chargebacks	Discounts and Distributor Fees	Total
Balance at December 31, 2021	\$ 195,715	\$ 15,814	\$ 11,389	\$ 21,808	\$ 244,726
Provision, net	630,295	13,222	135,854	186,609	965,980
Payments/credits	(528,209)	(2,872)	(132,622)	(190,062)	(853,765)
Balance at December 31, 2022	297,801	26,164	14,621	18,355	356,941
Provision, net	651,209	2,485	185,886	179,688	1,019,268
Payments/credits	(640,566)	(8,214)	(185,575)	(174,814)	(1,009,169)
Balance at December 31, 2023	308,444	20,435	14,932	23,229	367,040
Provision, net	820,865	15,883	212,389	189,071	1,238,208
Payments/credits	(810,782)	(9,890)	(214,896)	(174,067)	(1,209,635)
Balance at December 31, 2024	\$ 318,527	\$ 26,428	\$ 12,425	\$ 38,233	\$ 395,613

Total items deducted from gross product sales were \$1,238.2 million, \$1,019.3 million and \$966.0 million, or 24.5%, 21.4% and 21.0% as a percentage of gross product sales, in 2024, 2023 and 2022, respectively.

Included in these amounts are immaterial adjustments related to prior-year sales due to changes in estimates.

Rebates

We are subject to rebates on sales made under governmental managed-care pricing programs and commercial payor contracts in the U.S. The largest of these rebates is associated with sales covered by commercial payor contracts and Epidiolex Medicaid. We participate in state government-managed Medicaid programs as well as certain other qualifying federal and state government programs under the terms of which discounts and rebates are provided to participating government entities. We offer rebates and discounts to managed health care organizations and commercial payors in the U.S. In estimating our provisions for rebates, we consider relevant statutes with respect to governmental pricing programs and contractual sales terms with managed-care providers, commercial payors and group purchasing organizations. We estimate the rebate provision based on historical utilization rates, historical payment experience, new information regarding changes in regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates and channel inventory data obtained from our major distributors in accordance with our inventory management agreements. Estimating these rebates is complex, in part due to the time delay between the date of sale and the actual settlement of the liability. We believe that the methodology we use to estimate rebates on product sales made under governmental managed-care pricing programs and commercial payor contracts is reasonable and appropriate given current facts and circumstances. However, estimates may vary from actual experience.

Rebates were \$820.9 million, \$651.2 million and \$630.3 million, or 16.2%, 13.7% and 13.7% as a percentage of gross product sales, in 2024, 2023 and 2022, respectively. Rebates as a percentage of gross product sales in 2024 increased compared to 2023, primarily due to higher rebate rates with commercial payors. Rebates as a percentage of gross product sales in 2023 were in line with 2022. Rebates as a percentage of gross product sales are expected to increase in 2025 compared to 2024, primarily due to higher rebate rates in commercial payor contracts.

Sales returns

For certain products, we allow customers to return product within a specified period before and after the applicable expiration date and issue credits which may be applied against existing or future invoices. We account for sales returns as a reduction in net revenue at the time a sale is recognized by establishing an accrual in an amount equal to the estimated value of products expected to be returned. The sales return accrual is estimated principally based on historical experience, the level and estimated shelf life of inventory in the distribution channel, our return policy and expected market events including generic competition.

Sales returns were \$15.9 million, \$2.5 million and \$13.2 million, or 0.3%, 0.1% and 0.3% as a percentage of gross product sales in 2024, 2023 and 2022, respectively. Sales returns as a percentage of gross product sales are not expected to change materially in 2025 compared to 2024.

Chargebacks

We participate in chargeback programs with a number of entities, principally Federal Supply Schedule, Group Purchasing Organizations, and other public parties, under which pricing on products below wholesalers' list prices is provided to participating entities. These entities purchase product through wholesalers at the contract price and the wholesalers charge back to us the difference between their acquisition cost and the lower negotiated price. We record the difference as allowances

against accounts receivable. We determine our estimate of the chargebacks provision primarily based on historical experience on a product and program basis, current contract prices under the chargeback programs and channel inventory data.

Chargebacks were \$212.4 million, \$185.9 million and \$135.9 million, or 4.2%, 3.9% and 2.9% as a percentage of gross product sales in 2024, 2023 and 2022, respectively. Chargebacks as a percentage of gross product sales increased in 2024 compared to 2023, primarily due to higher chargeback utilization. Chargebacks as a percentage of gross product sales increased in 2023 compared to 2022, primarily due to higher chargeback utilization. Chargebacks as a percentage of gross product sales are not expected to change materially in 2025 compared to 2024.

Discounts and distributor fees

Discounts and distributor fees comprise prompt payment discounts, patient coupon programs and specialty distributor and wholesaler fees. We offer customers a cash discount on gross product sales as an incentive for prompt payment. We estimate provisions for prompt pay discounts based on contractual sales terms with customers and historical payment experience. To help patients afford our products, we have various programs to assist them, including patient assistance programs, a free product voucher program and co-pay coupon programs for certain products. We estimate provisions for these programs primarily based on expected program utilization, adjusted as necessary to reflect our actual experience on a product and program basis. Specialty distributor and wholesaler fees comprise fees for distribution of our products. We estimate provisions for distributor and wholesaler fees primarily based on sales volumes and contractual terms with our distributors.

Discounts and distributor fees were \$189.1 million, \$179.7 million and \$186.6 million, or 3.7%, 3.8% and 4.1% as a percentage of gross product sales in 2024, 2023 and 2022, respectively. Discounts and distributor fees as a percentage of gross product sales in 2024 were in line with 2023. Discounts and distributor fees as a percentage of gross product sales in 2023 were broadly in line with 2022. Discounts and distributor fees as a percentage of gross product sales are not expected to change materially in 2025 compared to 2024.

Acquisitions and Valuation of Intangibles

We make certain judgments to determine whether transactions should be accounted for as acquisitions of assets or as business combinations. If it is determined that substantially all of the fair value of gross assets acquired in a transaction is concentrated in a single asset (or a group of similar assets), the transaction is treated as an acquisition of assets. We evaluate the inputs, processes, and outputs associated with the acquired set of activities. If the assets in a transaction include an input and a substantive process that together significantly contribute to the ability to create outputs, the transaction is treated as an acquisition of a business.

We account for business combinations using the acquisition method of accounting, which requires that assets acquired and liabilities assumed generally be recorded at their fair values as of the acquisition date. Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. In performing the annual impairment test, the fair value of the reporting unit is compared to its corresponding carrying value, including goodwill. If the carrying value exceeds the fair value of the reporting unit an impairment loss will be recognized for the amount by which the reporting unit's carrying amount exceeds its fair value, not to exceed the carrying amount of goodwill. We have determined the fair value of our single reporting unit to be equal to our market capitalization, as determined by our traded share price, plus a control premium. The control premium used was based on a review of such premiums identified in recent acquisitions of companies of similar size and in similar industries. We performed our annual goodwill impairment test in October 2024 and concluded that goodwill was not impaired as the fair value of the reporting unit significantly exceeded its carrying amount, including goodwill. As of December 31, 2024, we had \$1.7 billion of goodwill resulting from acquisitions accounted for as business combinations.

In transactions accounted for as acquisitions of assets, no goodwill is recorded and contingent consideration such as payments upon achievement of various developmental, regulatory and commercial milestones generally is not recognized at the acquisition date. In an asset acquisition, upfront payments allocated to IPR&D projects at the acquisition date are expensed unless there is an alternative future use. In addition, product development milestones are expensed upon achievement.

Valuation of Intangible Assets

We have acquired, and expect to continue to acquire, intangible assets through asset acquisitions or business combinations. When significant identifiable intangible assets are acquired, we engage an independent third party valuation firm to assist in determining the fair values of these assets as of the acquisition date. Discounted cash flow models are typically used in these valuations, which require the use of significant estimates and assumptions, including but not limited to:

- estimating the timing of and expected costs to complete the in-process projects;
- projecting regulatory approvals;

- estimating future cash flows including revenues and operating profits resulting from completed products and in-process projects; and
- developing appropriate discount rates and probability rates by project.

We believe the fair values that we assign to the intangible assets acquired are based upon reasonable estimates and assumptions given available facts and circumstances as of the acquisition dates. No assurance can be given, however, that the underlying assumptions used to estimate expected cash flows will transpire as estimated. In addition, we are required to estimate the period of time over which to amortize the intangible assets, which requires significant judgment.

Impairment of Intangible Assets

Finite-lived intangible assets consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from seven to sixteen years. The estimated useful lives associated with intangible assets are consistent with the estimated lives of the products and may be modified when circumstances warrant. Intangible assets with finite lives are reviewed for impairment whenever events or circumstances indicate that the carrying value of an asset may not be recoverable. Events giving rise to impairment are an inherent risk in the pharmaceutical industry and cannot be predicted. Factors that we consider in deciding when to perform an impairment review include significant under-performance of a product in relation to expectations, significant negative industry or economic trends, and significant changes or planned changes in our use of the assets. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. Estimating future cash flows related to an intangible asset involves estimates and assumptions. If our assumptions are not correct, there could be an impairment loss or, in the case of a change in the estimated useful life of the asset, a change in amortization expense.

IPR&D is not amortized but is tested for impairment annually or when events or circumstances indicate that the fair value may be below the carrying value of the asset. If the carrying value of the assets is not expected to be recovered, the assets are written down to their estimated fair values.

As of December 31, 2024, we had \$4.8 billion of finite-lived intangible assets, of which \$3.3 billion related to the Epidiolex intangible asset which we acquired in the GW Acquisition and \$1.0 billion related to the Vyxeos intangible asset which we acquired in the Celator Acquisition. As part of our annual impairment assessment, we reviewed these intangible assets as of December 31, 2024 and determined the carrying value is recoverable. Cash flow models used in our assessment are based on our commercial experience to date and require the use of significant estimates, which include, but are not limited to, patient-related assumptions, including patient population and segmentation, patient growth and treatment rates, and long-range pricing expectations.

We did not recognize an impairment charge related to our intangible assets in 2024 or 2023. In 2022, we recorded an acquired IPR&D asset impairment charge of \$133.6 million as a result of the decision to discontinue our nabiximols program.

Please refer to Note 9, Goodwill and Intangible Assets, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K, for further information about our intangible assets and the remaining useful lives of our finite-lived intangible assets as of December 31, 2024.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. We provide a valuation allowance when it is more-likely-than-not that deferred tax assets will not be realized.

Our most significant tax jurisdictions are Ireland, the U.K. and the U.S. Certain estimates are required in determining our expense for income taxes. Some of these estimates are based on management's interpretations of jurisdiction-specific tax laws or regulations and the likelihood of settlement related to tax audit issues. Various internal and external factors may have favorable or unfavorable effects on our future effective income tax rate. These factors include, but are not limited to, changes in tax laws, regulations and/or rates, changing interpretations of existing tax laws or regulations, changes in estimates of prior years' items, the impact of accounting for share-based compensation, changes in our international organization, likelihood of settlement, and changes in overall levels of income before taxes.

Realization of our deferred tax assets is dependent upon the generation of future taxable income, the amount and timing of which are uncertain. In evaluating our ability to recover our deferred tax assets, we consider all available positive and negative evidence, including cumulative income in recent fiscal years, our forecast of future taxable income exclusive of certain reversing temporary differences and significant risks and uncertainties related to our business. In determining future taxable income, we are responsible for assumptions utilized including the amount of state, federal and international pre-tax operating income, the reversal of certain temporary differences and the implementation of feasible and prudent tax planning strategies.

These assumptions require significant judgment about the forecasts of future taxable income in applicable tax jurisdictions, which are based on our commercial experience to date and are consistent with the plans and estimates that we are using to manage our underlying business.

We maintain a valuation allowance against certain other deferred tax assets where realizability is not certain. We periodically evaluate the likelihood of the realization of deferred tax assets and reduce the carrying amount of these deferred tax assets by a valuation allowance to the extent we believe a portion will not be realized. This determination depends on a variety of factors, some of which are subjective, including our recent cumulative earnings experience by taxing jurisdiction, expectations of future taxable income, carryforward periods available to us for tax reporting purposes, various income tax strategies and other relevant factors. If we determine that the deferred tax assets are not realizable in a future period, we would record material changes to income tax expense in that period.

We have also provided for unrecognized tax benefits that we believe are not more-likely-than-not to be sustained upon examination by tax authorities. The evaluation of unrecognized tax benefits is based on factors that include, but are not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate unrecognized tax benefits on a quarterly basis and adjust the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Our liabilities for unrecognized tax benefits can be relieved only if the contingency becomes legally extinguished through either payment to the taxing authority or the expiration of the statute of limitations, the recognition of the benefits associated with the position meet the more-likely-than-not threshold or the liability becomes effectively settled through the examination process. We consider matters to be effectively settled once the taxing authority has completed all of its required or expected examination procedures, including all appeals and administrative reviews. We also accrue for potential interest and penalties related to unrecognized tax benefits in income tax expense.

Recent Accounting Pronouncements

For a discussion of recent accounting pronouncements, please see Note 2, Summary of Significant Accounting Policies, of the Notes to Consolidated Financial Statements included in Part IV of this Annual Report on Form 10-K.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk. The primary objectives of our investment policy, in order of priority, are as follows: safety and preservation of principal and diversification of risk; liquidity of investments sufficient to meet cash flow requirements; and competitive yield. Although our investments are subject to market risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or certain types of investment. Our investment policy allows us to maintain a portfolio of cash equivalents and short-term investments in a variety of securities, including U.S. federal government and federal agency securities, corporate bonds or commercial paper issued by U.S. corporations, money market instruments, certain qualifying money market mutual funds, certain repurchase agreements, and tax-exempt obligations of states, agencies and municipalities in the U.S. Our cash equivalents and investments as of December 31, 2024 consisted of money market funds and time deposits which are not subject to significant interest rate risk.

We are exposed to risks associated with changes in interest rates in connection with our term loan borrowings. In May 2021 we entered into the Credit Agreement which provided for (i) the Dollar Term Loan, (ii) the Euro Term Loan and (iii) the Initial Revolving Credit Facility. In January 2024, we entered into the Repricing Amendment No. 1 to the Credit Agreement. Upon entry into the Repricing Amendment No. 1, certain existing lenders converted a portion of the outstanding Dollar Term Loan into the Tranche B-1 Dollar Term Loans and we borrowed \$201.9 million aggregate principal amount of additional Tranche B-1 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Dollar Term Loan that was not converted. In July 2024, we entered into the Repricing Amendment No. 2 to the Credit Agreement, as amended by the Repricing Amendment No. 1. Upon entry into the Repricing Amendment No. 2, certain existing lenders converted a portion of the outstanding Tranche B-1 Dollar Term Loans into the Tranche B-2 Dollar Term Loans and we borrowed \$289.6 million aggregate principal amount of additional Tranche B-2 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Tranche B-1 Dollar Term Loans that were not converted. In November 2024, we entered into Amendment No. 3 to the Credit Agreement, as amended by the Repricing Amendment No. 1 and Repricing Amendment No. 2, to increase the Initial Revolving Credit Facility from \$500.0 million to \$885.0 million and extend the maturity date from May 5, 2026 to November 26, 2029.

There were no borrowings outstanding under the Amended Revolving Credit Facility or the Euro Term Loan as of December 31, 2024. Tranche B-2 Dollar Term Loans borrowings of \$2.7 billion were outstanding as of December 31, 2024 and subject to an either (a) Term SOFR, or (b) the prime lending rate, in each case, plus an applicable margin. The applicable margin for the Tranche B-2 Dollar Term Loans is 2.25% (in the case of Term SOFR borrowings) and 1.25% (in the case of borrowings at the prime lending rate). To achieve a desired mix of floating and fixed interest rates on our Tranche B-2 Dollar

Term Loans, we entered into interest rate swap agreements in April 2023. The interest rate swap agreements have a notional amount of \$500.0 million and are effective until April 2026. As a result of these agreements, the interest rate on a portion of our term loan borrowings is fixed at 3.9086%, plus the borrowing spread, until April 30, 2026. The net asset fair value of outstanding interest rate swap contracts was \$1.0 million as of December 31, 2024. The impact of a hypothetical increase or decrease in interest rates on the fair value of the interest rate swap contracts would be offset by a change in the value of the underlying liability. If interest rates were to increase or decrease by 1%, interest expense for 2025 would increase or decrease by approximately \$15.5 million, based on the unhedged portion of our outstanding variable rate borrowings.

In September 2024, we completed a private placement of \$1.0 billion aggregate principal amount of the 2030 Notes. In April 2021, we issued \$1.5 billion in aggregate principal amount of the Secured Notes. In June 2020, we completed a private placement of \$1.0 billion aggregate principal amount of the 2026 Notes.

The 2030 Notes, the Secured Notes and the 2026 Notes have fixed annual interest rates of 3.125%, 4.375% and 2.000%, respectively, and we therefore do not have economic interest rate exposure on the 2030 Notes, the Secured Notes and the 2026 Notes. However, the fair values of the 2030 Notes, the Secured Notes and the 2026 Notes are exposed to interest rate risk. Generally, the fair values of the 2030 Notes, the Secured Notes and the 2026 Notes will increase as interest rates fall and decrease as interest rates rise. The fair values of the 2030 Notes and the 2026 Notes are also affected by volatility in our ordinary share price. As of December 31, 2024, the fair values of the 2030 Notes, the Secured Notes and the 2026 Notes were estimated to be \$1.1 billion, \$1.4 billion and \$1.0 billion, respectively.

Foreign Currency Exchange Rate Risk. We have significant operations in Europe as well as in the U.S. The functional currency of each foreign subsidiary is generally the local currency. We are exposed to foreign currency exchange risk as the functional currency financial statements of foreign subsidiaries are translated to U.S. dollars. The assets and liabilities of our foreign subsidiaries having a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date, and at the average exchange rate for the reporting period for revenue and expense accounts. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive loss in shareholders' equity. The reported results of our foreign subsidiaries will be influenced by their translation into U.S. dollars by currency movements against the U.S. dollar. Our primary currency translation exposure is related to our subsidiaries that have functional currencies denominated in sterling and euro. A hypothetical 10% strengthening or weakening in the rates used to translate the results of our foreign subsidiaries that have functional currencies denominated in sterling and euro would have increased or decreased net income for the year ended December 31, 2024 by approximately \$78.0 million and \$3.3 million, respectively.

Transactional exposure arises where transactions occur in currencies other than the functional currency. Transactions in foreign currencies are recorded at the exchange rate prevailing at the date of the transaction. The resulting monetary assets and liabilities are translated into the appropriate functional currency at exchange rates prevailing at the balance sheet date and the resulting gains and losses are reported in foreign exchange gain (loss) in the consolidated statements of income (loss). As of December 31, 2024, our exposure to transaction risk primarily related to sterling and euro denominated net monetary liabilities, including intercompany loans, held by subsidiaries with a U.S. dollar functional currency. We have entered into foreign exchange forward contracts to manage this currency risk. These foreign exchange forward contracts are not designated as hedges; gains and losses on these derivative instruments are designed to offset gains and losses on the underlying balance sheet exposures. As of December 31, 2024, we held foreign exchange forward contracts with notional amounts totaling \$461.2 million. The net liability fair value of outstanding foreign exchange forward contracts was \$7.9 million as of December 31, 2024. Based on our foreign currency exchange rate exposures as of December 31, 2024, a hypothetical 10% adverse fluctuation in exchange rates would decrease the fair value of our foreign exchange forward contracts by approximately \$6.9 million. The resulting loss on these forward contracts would be offset by a positive impact on the underlying monetary assets and liabilities.

Item 8. Financial Statements and Supplementary Data

Our consolidated financial statements as listed below are included in this Annual Report on Form 10-K as pages F-1 through F-51.

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Jazz Pharmaceuticals plc	
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Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures. We have carried out an evaluation under the supervision and with the participation of management, including our principal executive officer and principal financial officer, of our disclosure controls and procedures (as defined in Rule 13a-15(e) and 15d-15(e) of the Exchange Act) as of the end of the period covered by this Annual Report on Form 10-K. Based on their evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures were effective as of December 31, 2024.

Limitations on the Effectiveness of Controls. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues, if any, within an organization have been detected. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure control system are met and, as set forth above, our principal executive officer and principal financial officer have concluded, based on their evaluation as of the end of the period covered by this report, that our disclosure controls and procedures were effective to provide reasonable assurance that the objectives of our disclosure control system were met.

Changes in Internal Control over Financial Reporting. During the quarter ended December 31, 2024, there were no changes to our internal control over financial reporting that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Management's Report on Internal Control over Financial Reporting. The following report is provided by management in respect of our internal control over financial reporting (as defined in Rule 13a-15(f) and 15d-15(f) of the Exchange Act):

1. Our management is responsible for establishing and maintaining adequate internal control over financial reporting.
2. Our management used the COSO framework to evaluate the effectiveness of internal control over financial reporting. Management believes that the COSO framework is a suitable framework for its evaluation of financial reporting because it is free from bias, permits reasonably consistent qualitative and quantitative measurements of our internal control over financial reporting, is sufficiently complete so that those relevant factors that would alter a conclusion about the effectiveness of our internal control over financial reporting are not omitted and is relevant to an evaluation of internal control over financial reporting.
3. Management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2024 and has concluded that such internal control over financial reporting was effective. There were no material weaknesses in internal control over financial reporting identified by management.
4. KPMG, our independent registered public accounting firm, has audited the consolidated financial statements of Jazz Pharmaceuticals plc as of and for the year ended December 31, 2024, included herein, and has issued an audit report on our internal control over financial reporting, which is included below.

To the Shareholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on Internal Control Over Financial Reporting

We have audited Jazz Pharmaceuticals plc and subsidiaries' (the Company) internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission. In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2024, based on criteria established in *Internal Control – Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2024 and 2023, the related consolidated statements of income (loss), comprehensive income (loss), shareholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2024, and the related notes and financial statement schedules at item 15(a)2 (collectively, 'the consolidated financial statements'), and our report dated February 26, 2025 expressed an unqualified opinion on those consolidated financial statements.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Managements Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ KPMG

Dublin, Ireland
February 26, 2025

Item 9B. Other Information**Insider Trading Arrangements**

The following is a summary of the material terms of the contracts, instructions or written plans for the purchase or sale of the Company's securities adopted or terminated by our officers (as defined in Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended) and directors during the quarter ended December 31, 2024:

Name and Position	Date	Type of Trading Arrangement		Rule 10b5-1*	Expiration Date	Total Ordinary Shares to be Sold
		Action				
Robert Iannone	December 6, 2024	Termination ⁽¹⁾		X	March 7, 2025	10,681
Robert Iannone	December 6, 2024	Adoption ⁽¹⁾		X	December 6, 2025	12,625
Executive Vice President, Global Head of Research and Development, Chief Medical Officer						

(1) Represents the modification, as described in Rule 10b5-1(c)(1)(iv) under the Exchange Act, of a written plan initially adopted on March 7, 2024 that was intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.

* Contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Securities Exchange Act of 1934, as amended.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections

Not applicable.

PART III

Certain information required by Part III is omitted from this Annual Report on Form 10-K and incorporated by reference to our 2025 Proxy Statement, to be filed pursuant to Regulation 14A of the Exchange Act. If our 2025 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 10. Directors, Executive Officers and Corporate Governance

The information required by this item is to be included in our 2025 Proxy Statement as follows and is incorporated by reference:

- The information relating to our directors and nominees for director is to be included in the section entitled "Proposal 1—Election of Directors;"
- The information relating to our executive officers is to be included in the section entitled "Executive Officers;"
- The information relating to our Audit Committee, audit committee financial expert, procedures by which shareholders may recommend nominees to our board of directors and our insider trading policies and procedures is to be included in the section entitled "Corporate Governance and Board Matters;" and
- If required, the information regarding compliance with Section 16(a) of the Exchange Act is to be included in the section entitled "Delinquent Section 16(a) Reports."

Such information is incorporated herein by reference to our 2025 Proxy Statement, provided that if the 2025 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Our Code of Conduct applies to all of our employees, directors and officers, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions, and those of our

subsidiaries. The Code of Conduct is available on our website at www.jazzpharmaceuticals.com under the section entitled “Our Purpose” under “Ethical Standards.” We intend to satisfy the disclosure requirements under Item 5.05 of the SEC Form 8-K regarding an amendment to, or waiver from, a provision of our Code of Conduct by posting such information on our website at the website address and location specified above.

Item 11. Executive Compensation

The information required by this item is to be included in our 2025 Proxy Statement under the sections entitled “Executive Compensation,” “Director Compensation,” “Corporate Governance and Board Matters—Compensation Committee Interlocks and Insider Participation” and “Corporate Governance and Board Matters—Compensation Committee Report” and is incorporated herein by reference, provided that if the 2024 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item with respect to equity compensation plans is to be included in our 2025 Proxy Statement under the section entitled “Equity Compensation Plan Information” and the information required by this item with respect to security ownership of certain beneficial owners and management is to be included in our 2025 Proxy Statement under the section entitled “Security Ownership of Certain Beneficial Owners and Management” and in each case is incorporated herein by reference, provided that if the 2025 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is to be included in our 2025 Proxy Statement under the sections entitled “Certain Relationships and Related Party Transactions” and “Corporate Governance and Board Matters—Independence of the Board of Directors” and is incorporated herein by reference, provided that if the 2025 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

Item 14. Principal Accountant Fees and Services

The information required by this item is to be included in our 2025 Proxy Statement under the section entitled “Proposal 2—On a Non-Binding Advisory Basis, Ratify Appointment of Independent Registered Accounting Firm and, On a Binding Basis, Authorize the Board of Directors, Acting Through the Audit Committee, to Determine the Independent Auditors’ Remuneration” and is incorporated herein by reference, provided that if the 2025 Proxy Statement is not filed within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K, the omitted information will be included in an amendment to this Annual Report on Form 10-K filed not later than the end of such 120-day period.

PART IV**Item 15. Exhibits and Financial Statement Schedules**

(a) *The following documents are filed as part of this Annual Report on Form 10-K:*

1. Financial Statements:

See Consolidated Financial Statements in Part II, Item 8 of this Annual Report on Form 10-K.

2. Financial Statement Schedules:

The following financial statement schedule of Jazz Pharmaceuticals plc is filed as part of this Annual Report on Form 10-K on page F-51 and should be read in conjunction with the consolidated financial statements of Jazz Pharmaceuticals plc.

Schedule II: Valuation and Qualifying Accounts

All other schedules are omitted because they are not applicable, not required under the instructions, or the requested information is shown in the consolidated financial statements or related notes thereto.

(b) Exhibits—The following exhibits are included herein or incorporated herein by reference:

<u>Exhibit Number</u>	<u>Description of Document</u>
2.1	Agreement and Plan of Merger and Reorganization, dated as of September 19, 2011, by and among Azur Pharma Limited (now Jazz Pharmaceuticals plc), Jaguar Merger Sub Inc., Jazz Pharmaceuticals, Inc. and Seamus Mulligan, solely in his capacity as the Indemnitors' Representative (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500) filed with the SEC on September 19, 2011).
2.2	Agreement and Plan of Merger, dated as of May 27, 2016, by and among Jazz Pharmaceuticals plc, Plex Merger Sub, Inc., and Celator Pharmaceuticals, Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on May 31, 2016).
2.3†	Transaction Agreement, dated as of February 3, 2021, by and among Jazz Pharmaceuticals UK Holdings Limited, Jazz Pharmaceuticals Public Limited Company and GW Pharmaceuticals PLC (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on February 4, 2021).
2.4#	License and Collaboration Agreement, dated October 18, 2022, between Jazz Pharmaceuticals Ireland Limited and Zymeworks BC Inc. (incorporated herein by reference to Exhibit 2.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on December 5, 2022).
3.1	Amended and Restated Memorandum and Articles of Association of Jazz Pharmaceuticals plc, as amended on August 4, 2016 (incorporated herein by reference to Exhibit 3.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
4.1	Reference is made to Exhibit 3.1.
4.2A	Investor Rights Agreement, dated July 7, 2009 by and between Jazz Pharmaceuticals, Inc. and the other parties named therein (incorporated herein by reference to Exhibit 10.88 in Jazz Pharmaceuticals, Inc.'s Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on July 7, 2009).
4.2B	Assignment, Assumption and Amendment Agreement, dated as of January 18, 2012, by and among Jazz Pharmaceuticals, Inc., Jazz Pharmaceuticals plc and the other parties named therein (incorporated herein by reference to Exhibit 4.7B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals, Inc. with the SEC on February 28, 2012).
4.3A	Indenture, dated as of August 23, 2017, among Jazz Pharmaceuticals Public Limited Company, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 23, 2017).
4.3B	Form of 1.50% Exchangeable Senior Note due 2024 (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on August 23, 2017).
4.4A	Indenture, dated as of June 11, 2020 among Jazz Pharmaceuticals Public Limited Company, Jazz Investments I Limited and U.S. Bank National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on June 11, 2020).
4.4B	Form of 2.000% Exchangeable Senior Note due 2026 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on June 11, 2020).
4.5A	Indenture, dated as of April 29, 2021, among Jazz Securities Designated Activity Company, the guarantors party thereto, U.S. Bank National Association, as trustee and acknowledged by U.S. Bank National Association, as collateral trustee (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on April 29, 2021).
4.5B	Form of 4.375% Senior Notes due 2029 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on April 29, 2021).

4.5C	First Supplemental Indenture, dated as of July 21, 2021, among GW Pharmaceuticals Limited, GW Global Services (International) Limited, GW Pharma Limited, GW Research Limited, GW UK Services Limited and Greenwich Biosciences, Inc., Jazz Securities Designated Activity Company, and U.S. Bank National Association, as trustee under the Indenture, dated as of April 29, 2021 (incorporated herein by reference to Exhibit 4.5C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
4.5D	Indenture, dated as of September 6, 2024 among Jazz Pharmaceuticals Public Limited Company, Jazz Investments I Limited and U.S. Bank Trust Company, National Association (incorporated herein by reference to Exhibit 4.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on September 6, 2024).
4.5E	Form of 3.125% Exchangeable Senior Note due 2030 (incorporated herein by reference to Exhibit 4.2 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on September 6, 2024).
4.6	Description of Share Capital.
10.1A	Credit Agreement, dated as of May 5, 2021, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers from time to time party thereto, the lenders and issuing banks from time to time party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank National Association, as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on May 5, 2021).
10.1B	Conforming Changes Amendment, dated as of June 7, 2023, entered into by Bank of America, N.A. as administrative agent to Credit Agreement, dated as of May 5, 2021, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers from time to time party thereto, the lenders and issuing banks from time to time party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank National Association, as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2023, as filed with the SEC on August 9, 2023).
10.1C	Amendment No. 1, dated as of January 19, 2024, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers from time to time party thereto, the lenders and issuing banks from time to time party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank Trust Company, National Association, as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on January 25, 2024).
10.1D	Amendment No. 2, dated as of January 19, 2024, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers party thereto, the guarantors party thereto, the lenders party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank Trust Company, National Association, (as successor in interest to U.S. Bank National Association), as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on July 22, 2024).
10.2	Amendment No. 3, dated as of November 26, 2024, by and among Jazz Pharmaceuticals Public Limited Company, the other borrowers party thereto, the guarantors party thereto, the lenders and issuing banks party thereto, Bank of America, N.A., as administrative agent, and U.S. Bank Trust Company, National Association (as successor in interest to U.S. Bank National Association), as collateral trustee (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-033500), as filed with the SEC on November 26, 2024).
10.3#	Settlement Agreement, dated as of April 5, 2017, by and between Jazz Pharmaceuticals, Inc. and Jazz Pharmaceuticals Ireland Limited, and Roxane Laboratories, Inc., West-Ward Pharmaceuticals Corp., Eurohealth (USA), Inc., and Hikma Pharmaceuticals PLC (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2022, as filed with the SEC on November 9, 2022).
10.4†	Supply Agreement, dated as of April 1, 2010, by and between Jazz Pharmaceuticals, Inc. and Siegfried (USA) Inc. (incorporated herein by reference to Exhibit 10.54 in Jazz Pharmaceuticals, Inc.'s Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2010, as filed with the SEC on May 6, 2010).
10.5‡	Master Manufacturing Services Agreement, dated as of October 1, 2015, by and between Jazz Pharmaceuticals Ireland Limited and Patheon Pharmaceuticals Inc. (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.6‡	Contract Manufacturing Agreement, dated as of January 20, 2020, by and between Jazz Pharmaceuticals Ireland Limited and Siegfried AG (incorporated herein by reference to Exhibit 10.10 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).

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10.7#	Pharmacy Master Services Agreement, dated as of December 1, 2022, by and between Jazz Pharmaceuticals, Inc. and Express Scripts Specialty Distribution Services, Inc. (incorporated herein by reference to Exhibit 10.8# in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2022, as filed with the SEC on March 1, 2023).
10.8A‡	Amended and Restated License Agreement, dated as of October 14, 2020, between Pharma Mar, S.A. and Jazz Pharmaceuticals Ireland Limited (incorporated herein by reference to Exhibit 10.12 in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.8B‡	Amendment No. 1, dated as of May 6, 2021, to Amended and Restated License Agreement, dated as of October 14, 2020, between Pharma Mar, S.A. and Jazz Pharmaceuticals Ireland Limited (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals, plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.9	Lease, dated May 8, 2012, by and between John Ronan and Castle Cove Property Developments Limited and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2012, as filed with the SEC on August 7, 2012).
10.10+	Form of Indemnification Agreement between Jazz Pharmaceuticals plc and its officers and directors (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Current Report on Form 8-K (File No. 001-33500), as filed with the SEC on January 18, 2012).
10.11+	Offer Letter from Jazz Pharmaceuticals, Inc. to Robert Iannone dated as of April 11, 2019 (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2019, as filed with the SEC on August 6, 2019).
10.12A+	Employment Agreement, dated as of May 16, 2012 by and between Patricia Carr and Jazz Pharmaceuticals plc (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.12B+	Change in Control Severance Terms, dated as of May 15, 2016, by and between Jazz Pharmaceuticals Ireland Ltd. and Patricia Carr (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.12C+	Change in Control Stock Award Acceleration Agreement, dated as of May 15, 2016 by and between Jazz Pharmaceuticals plc and Patricia Carr (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.13+	Offer Letter, dated as of July 5, 2019 by and between Jazz Pharmaceuticals, Inc. and Neena M. Patil (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2019, as filed with the SEC on November 5, 2019).
10.14A+	Employment Contract, dated as of December 14, 2019, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.28A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.14B+	Equity Award Letter, dated as of December 9, 2019, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.28B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.14C+	Amendment to Employment Contract, dated as of April 21, 2020, by and between Jazz Pharmaceuticals UK Limited and Samantha Pearce (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2020, as filed with the SEC on May 5, 2020).
10.14D+	Offer Letter from Jazz Pharmaceuticals, Inc. to Samantha Pearce (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2024, as filed with the SEC on August 1, 2024).
10.15+	Offer Letter, dated as of February 23, 2020, by and between Jazz Pharmaceuticals, Inc. and Renée Galá (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2020, as filed with the SEC on May 5, 2020).

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10.16A+	Offer Letter, dated as of April 4, 2023, by and between Jazz Pharmaceuticals Ireland and Liz Henderson (incorporated herein by reference to Exhibit 10.17A in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).
10.16B+	New Hire Equity Letter, dated as of April 4, 2023, from Jazz Pharmaceuticals to Liz Henderson (incorporated herein by reference to Exhibit 10.17B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).
10.17A+	Offer Letter, dated as of January 30, 2024, by and between Jazz Pharmaceuticals, Inc. and Philip Johnson (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2024, as filed with the SEC on May 2, 2024).
10.17B+	Sign-On Bonus Repayment Agreement, dated as of February 25, 2024, by and between Jazz Pharmaceuticals, Inc. and Philip Johnson.
10.18A+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 99.1 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.18B+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan Sub-Plan Governing Awards to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.39B in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2011, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2012).
10.18C+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of U.S. Option Grant Notice and Form of U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18D+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved July 31, 2013) (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.18E+	Jazz Pharmaceuticals plc 2011 Equity Incentive Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2016, as filed with the SEC on May 10, 2016).
10.18F+	Amended and Restated 2011 Equity Incentive Plan (approved August 4, 2016) (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
10.18G+	Amended and Restated 2011 Equity Incentive Plan (approved November 3, 2016) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.18H+	Amended and Restated 2011 Equity Incentive Plan (approved November 2, 2022) (incorporated herein by reference to Exhibit 10.26Q+ in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2022, as filed with the SEC on March 1, 2023).
10.18I+	Amended and Restated 2011 Equity Incentive Plan (approved November 1, 2023) (incorporated herein by reference to Exhibit 10.18I in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).
10.18J+	Form of U.S. Option Grant Notice and Form of U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.18K+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).

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10.18L+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2018, as filed with the SEC on August 7, 2018).
10.18M+	Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.4 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.18N+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).
10.18O+	Form of U.S. Restricted Stock Unit Award Grant Notice and Form of U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.8 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.18P+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.18Q+	Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.1 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2021, as filed with the SEC on November 9, 2021).
10.18R+	Form of U.S. Performance Restricted Stock Unit Award Grant Notice and Form of U.S. Performance Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.6 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.18S+	Form of Non-U.S. Performance Restricted Stock Unit Award Grant Notice and Form of Non-U.S. Performance Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2011 Equity Incentive Plan (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).
10.19A+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 99.4 in Jazz Pharmaceuticals plc's registration statement on Form S-8 (File No. 333-179075), as filed with the SEC on January 18, 2012).
10.19B+	Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan (incorporated herein by reference to Exhibit 10.30B in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).
10.19C+	Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Option Plan - Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement (approved August 1, 2013) (incorporated herein by reference to Exhibit 10.7 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2013, as filed with the SEC on November 5, 2013).
10.19D+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved August 4, 2016) (incorporated herein by reference to Exhibit 10.9 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2016, as filed with the SEC on August 9, 2016).
10.19E+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved November 3, 2016) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).
10.19F+	Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved July 30, 2020) (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2020, as filed with the SEC on August 4, 2020).

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10.19G+	<u>Amended and Restated 2007 Non-Employee Directors Stock Award Plan (approved July 28, 2020) (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2024, as filed with the SEC on May 2, 2024).</u>
10.19H+	<u>Form of Non-U.S. Option Grant Notice and Form of Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated Non-Employee Directors 2007 Stock Award Plan (incorporated herein by reference to Exhibit 10.5 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2016, as filed with the SEC on November 8, 2016).</u>
10.19I+	<u>Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2018, as filed with the SEC on November 6, 2018).</u>
10.19J+	<u>Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2019, as filed with the SEC on May 7, 2019).</u>
10.19K+	<u>Form of Non-U.S. Option Grant Notice and Non-U.S. Option Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.2 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2020, as filed with the SEC on November 2, 2020).</u>
10.19L+	<u>Form of Non-U.S. Restricted Stock Unit Award Grant Notice and Non-U.S. Restricted Stock Unit Award Agreement under the Jazz Pharmaceuticals plc Amended and Restated 2007 Non-Employee Directors Stock Award Plan (incorporated herein by reference to Exhibit 10.3 in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended September 30, 2020, as filed with the SEC on November 2, 2020).</u>
10.20A+	<u>Amended and Restated GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.20A in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).</u>
10.20B+	<u>Form of Restricted Stock Unit Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10B in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).</u>
10.20C+	<u>Form of Replacement Stock Option Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).</u>
10.20D+	<u>Form of Replacement Restricted Stock Unit Award Agreement under the GW Pharmaceuticals plc 2020 Long-Term Incentive Plan (incorporated herein by reference to Exhibit 10.10D in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2021, as filed with the SEC on August 3, 2021).</u>
10.21A+	<u>Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan, as amended and restated (incorporated herein by reference to Exhibit 10.31A in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2012, as filed with the SEC on February 26, 2013).</u>
10.21B+	<u>Amended and Restated 2007 Employee Stock Purchase Plan (approved November 2, 2022) (incorporated herein by reference to Exhibit 10.30B+ in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2022, as filed with the SEC on March 1, 2023).</u>
10.21C+	<u>Amended and Restated 2007 Employee Stock Purchase Plan (approved November 1, 2023) (incorporated herein by reference to Exhibit 10.21C in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).</u>
10.21D+	<u>Jazz Pharmaceuticals plc 2007 Employee Stock Purchase Plan Sub-Plan Governing Purchase Rights to Participants in the Republic of Ireland (incorporated herein by reference to Exhibit 10.14C in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended March 31, 2012, as filed with the SEC on May 8, 2012).</u>

10.22A+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved October 30, 2019) (incorporated herein by reference to Exhibit 10.34C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.22B+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2020) (incorporated herein by reference to Exhibit 10.34D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2019, as filed with the SEC on February 25, 2020).
10.22C+	Jazz Pharmaceuticals plc Cash Bonus Plan for U.S. Affiliates (approved October 30, 2020) (incorporated herein by reference to Exhibit 10.33C in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.22D+	Jazz Pharmaceuticals Cash Bonus Plan (Ireland and Other Specified Affiliates) (Calendar Year 2021) (incorporated herein by reference to Exhibit 10.33D in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2020, as filed with the SEC on February 23, 2021).
10.22E+	Jazz Pharmaceuticals plc Global Cash Bonus Plan (approved November, 2021) (incorporated herein by reference to Exhibit 10.34E+ in Jazz Pharmaceuticals plc's Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2021, as filed with the SEC on March 1, 2022).
10.23+	Amended and Restated Executive Change in Control and Severance Benefit Plan, dated as of May 3, 2023 (incorporated herein by reference to Exhibit 10.2+ in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2023, as filed with the SEC on August 9, 2023).
10.24+	Amended and Restated Non-Employee Director Compensation Policy (approved May 4, 2023) (incorporated herein by reference to Exhibit 10.3+ in Jazz Pharmaceuticals plc's Quarterly Report on Form 10-Q (File No. 001-33500) for the period ended June 30, 2023, as filed with the SEC on August 9, 2023).
19.1	Jazz Pharmaceuticals plc Insider Trading Policy.
21.1	Subsidiaries of Jazz Pharmaceuticals plc.
23.1	Consent of KPMG, Independent Registered Public Accounting Firm.
24.1	Power of Attorney (included on the signature page hereto).
31.1	Certification of Principal Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of Principal Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1*	Certification of Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
97.1	Jazz Pharmaceuticals plc Policy for Recoupment of Incentive Compensation (incorporated herein by reference to Exhibit 97.1 in the Annual Report on Form 10-K (File No. 001-33500) for the period ended December 31, 2023, as filed by Jazz Pharmaceuticals plc on behalf of and as successor to Jazz Pharmaceuticals Inc. with the SEC on February 28, 2024).
101.INS	XBRL Instance Document - The instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

+ Indicates management contract or compensatory plan.

† Confidential treatment has been granted for portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

‡ Certain portions of this exhibit have been omitted pursuant to Item 601(b)(2) of Regulation S-K.

- # Portions of this document have been omitted pursuant to Item 601(b)(10) of Regulations S-K because they are both not material and are the type that the Company treats as private and confidential.
- * The certifications attached as Exhibit 32.1 accompany this Annual Report on Form 10-K pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended.

Item 16. Form 10-K Summary

None.

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: February 26, 2025

Jazz Pharmaceuticals public limited company
(Registrant)

/s/ BRUCE C. COZADD

Bruce C. Cozadd
Chairman, Chief Executive Officer and Director
(Principal Executive Officer)

/s/ PHILIP L. JOHNSON

Philip L. Johnson
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

/s/ PATRICIA CARR

Patricia Carr
Senior Vice President, Chief Accounting Officer
(Principal Accounting Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Bruce C. Cozadd, Philip L. Johnson, Neena M. Patil and Patricia Carr, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, the following persons on behalf of the registrant and in the capacities and on the dates indicated have signed this report below:

<u>Signature</u>	<u>Title</u>	<u>Date</u>
/s/ BRUCE C. COZADD Bruce C. Cozadd	Chairman, Chief Executive Officer and Director (Principal Executive Officer)	February 26, 2025
/s/ PHILIP L. JOHNSON Philip L. Johnson	Executive Vice President and Chief Financial Officer (Principal Financial Officer)	February 26, 2025
/s/ PATRICIA CARR Patricia Carr	Senior Vice President, Chief Accounting Officer (Principal Accounting Officer)	February 26, 2025
/s/ JENNIFER E. COOK Jennifer E. Cook	Director	February 26, 2025
/s/ PATRICK G. ENRIGHT Patrick G. Enright	Director	February 26, 2025
/s/ LAURA HAMILL Laura Hamill	Director	February 26, 2025
/s/ PATRICK KENNEDY Patrick Kennedy	Director	February 26, 2025
/s/ HEATHER ANN MCSHARRY Heather Ann McSharry	Director	February 26, 2025
/s/ SEAMUS C. MULLIGAN Seamus C. Mulligan	Director	February 26, 2025
/s/ KENNETH W. O'KEEFE Kenneth W. O'Keefe	Director	February 26, 2025
/s/ ANNE O'RIORDAN Anne O'Riordan	Director	February 26, 2025
/s/ NORBERT G. RIEDEL, PH.D. Norbert G. Riedel, Ph.D.	Director	February 26, 2025
/s/ MARK D. SMITH, M.D. Mark D. Smith, M.D.	Director	February 26, 2025
/s/ RICK E WINNINGHAM Rick E Winningham	Director	February 26, 2025

To the Shareholders and Board of Directors
Jazz Pharmaceuticals plc:

Opinion on the Consolidated Financial Statements

We have audited the accompanying consolidated balance sheets of Jazz Pharmaceuticals Plc and subsidiaries (the Company) as of December 31, 2024 and 2023, the related consolidated statements of income (loss), comprehensive income (loss), stockholders' equity, and cash flows for each of the years in the three-year period ended December 31, 2024 and the related notes and financial statement schedules at item 15(a)2 (collectively, the consolidated financial statements). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2024 and 2023, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2024, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2024, based on criteria established in Internal Control – Integrated Framework (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission", and our report dated February 26, 2025 expressed an unqualified opinion on the effectiveness of the Company's internal control over financial reporting.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these (consolidated) financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the consolidated financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matter or on the accounts or disclosures to which it relates.

Assessment of Epidiolex Medicaid Rebate Accrual

As discussed in Note 2 to the consolidated financial statements, sales made under governmental and managed-care pricing programs and commercial payor contracts in the U.S. are subject to rebates and requires significant judgment in determining the sales utilization percentage used in calculating the Epidiolex Medicaid rebate accrual. As discussed in Note 10 to the consolidated financial statements, the Company reported rebates and other sales deductions of \$342,717 thousands, which included rebates related to the Epidiolex Medicate rebate program in the U.S..

We identified the assessment of the Epidiolex Medicaid rebate accrual as a critical audit matter. Significant and complex auditor judgment was required to assess the Epidiolex Medicaid rebate accrual, specifically due to the significant judgment required in determining the sales utilization percentage used in the calculation of the Epidiolex Medicaid rebate accrual amount.

The following are the primary procedures we performed to address this critical audit matter.

- We evaluated the design and tested the operating effectiveness of certain internal controls related to the assessment of Epidiolex Medicaid rebate accrual.

- We compared the Company's historical Epidiolex Medicaid rebate accrual amount to the actual claims received to assess the Company's ability to accurately forecast.
- We assessed the assumption for reasonableness by comparing it against a sales utilization percentage range that was independently developed based on historical utilization rates.

/s/ KPMG

We have served as the Company's auditor since 2012.

Dublin, Ireland
February 26, 2025

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JAZZ PHARMACEUTICALS PLC
CONSOLIDATED BALANCE SHEETS
(In thousands, except per share amounts)

	December 31,	
	2024	2023
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 2,412,864	\$ 1,506,310
Investments	580,000	120,000
Accounts receivable, net of allowances of \$32,691 and \$21,136 at December 31, 2024 and 2023, respectively	716,765	705,794
Inventories	480,445	597,039
Prepaid expenses	177,411	185,476
Other current assets	261,543	320,809
Total current assets	4,629,028	3,435,428
Property, plant and equipment, net	173,413	169,646
Operating lease assets	53,582	65,340
Intangible assets, net	4,755,695	5,418,039
Goodwill	1,716,323	1,753,130
Deferred tax assets, net	560,245	477,834
Deferred financing costs	9,489	6,478
Other non-current assets	114,482	67,464
Total assets	\$ 12,012,257	\$ 11,393,359
LIABILITIES AND SHAREHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 77,869	\$ 102,750
Accrued liabilities	910,947	793,914
Current portion of long-term debt	31,000	604,954
Income taxes payable	18,757	35,074
Total current liabilities	1,038,573	1,536,692
Long-term debt, less current portion	6,077,640	5,107,988
Operating lease liabilities, less current portion	38,938	59,225
Deferred tax liabilities, net	676,736	847,706
Other non-current liabilities	86,614	104,751
Commitments and contingencies (Note 13)		
Shareholders' equity:		
Ordinary shares, nominal value \$0.0001 per share; 300,000 shares authorized; 60,631 and 62,255 shares issued and outstanding at December 31, 2024 and 2023, respectively	6	6
Non-voting euro deferred shares, €0.01 par value per share; 4,000 shares authorized, issued and outstanding at both December 31, 2024 and 2023	55	55
Capital redemption reserve	473	473
Additional paid-in capital	3,913,542	3,699,954
Accumulated other comprehensive loss	(947,667)	(842,147)
Retained earnings	1,127,347	878,656
Total shareholders' equity	4,093,756	3,736,997
Total liabilities and shareholders' equity	\$ 12,012,257	\$ 11,393,359

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF INCOME (LOSS)
(In thousands, except per share amounts)

	Year Ended December 31,		
	2024	2023	2022
Revenues:			
Product sales, net	\$ 3,821,164	\$ 3,736,943	\$ 3,641,429
Royalties and contract revenues	247,786	97,261	17,945
Total revenues	4,068,950	3,834,204	3,659,374
Operating expenses:			
Cost of product sales (excluding amortization of acquired developed technologies)	445,713	435,577	540,517
Selling, general and administrative	1,385,294	1,343,105	1,416,967
Research and development	884,000	849,658	590,453
Intangible asset amortization	627,313	608,284	599,169
Acquired in-process research and development	10,000	19,000	444,148
Intangible asset impairment charge	—	—	133,648
Total operating expenses	3,352,320	3,255,624	3,724,902
Income (loss) from operations	716,630	578,580	(65,528)
Interest expense, net	(238,097)	(289,438)	(288,242)
Foreign exchange gain (loss)	(8,182)	8,787	(19,014)
Income (loss) before income tax benefit and equity in loss of investees	470,351	297,929	(372,784)
Income tax benefit	(91,429)	(119,912)	(158,645)
Equity in loss of investees	1,660	3,009	9,921
Net income (loss)	\$ 560,120	\$ 414,832	\$ (224,060)
Net income (loss) per ordinary share:			
Basic	\$ 9.06	\$ 6.55	\$ (3.58)
Diluted	\$ 8.65	\$ 6.10	\$ (3.58)
Weighted-average ordinary shares used in per share calculations - basic	61,838	63,291	62,539
Weighted-average ordinary shares used in per share calculations - diluted	66,007	72,066	62,539

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(In thousands)

	Year Ended December 31,		
	2024	2023	2022
Net income (loss)	\$ 560,120	\$ 414,832	\$ (224,060)
Other comprehensive income (loss):			
Foreign currency translation adjustments	(106,025)	283,127	(725,277)
Loss on fair value hedging activities reclassified from accumulated other comprehensive loss to foreign exchange gain (loss), net of income tax benefit of \$—, \$—, and \$43, respectively	—	—	128
Unrealized gain on cash flow hedging activities, net of income tax expense of \$1,760, \$1,215 and \$—, respectively	5,298	3,658	—
Gain on cash flow hedging activities reclassified from accumulated other comprehensive loss to interest expense, net of income tax expense of \$1,593, \$1,137 and \$—, respectively	(4,793)	(3,423)	—
Other comprehensive income (loss)	(105,520)	283,362	(725,149)
Total comprehensive income (loss)	\$ 454,600	\$ 698,194	\$ (949,209)

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY—(Continued)
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2023	62,255	\$ 6	4,000	\$ 55	\$ 473	\$ 3,699,954	\$ (842,147)	\$ 878,656	\$ 3,736,997
Issuance of ordinary shares in conjunction with exercise of share options	22	—	—	—	—	1,629	—	—	1,629
Issuance of ordinary shares under employee stock purchase plan	212	—	—	—	—	19,018	—	—	19,018
Issuance of ordinary shares in conjunction with vesting of restricted stock units	892	—	—	—	—	—	—	—	—
Issuance of ordinary shares in conjunction with vesting of performance-based restricted stock units	80	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(57,753)	—	—	(57,753)
Share-based compensation	—	—	—	—	—	250,694	—	—	250,694
Shares repurchased	(2,830)	—	—	—	—	—	—	(311,429)	(311,429)
Other comprehensive loss	—	—	—	—	—	—	(105,520)	—	(105,520)
Net income	—	—	—	—	—	—	—	560,120	560,120
Balance at December 31, 2024	60,631	\$ 6	4,000	\$ 55	\$ 473	\$ 3,913,542	\$ (947,667)	\$ 1,127,347	\$ 4,093,756

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(In thousands)

	Ordinary Shares		Non-voting Euro Deferred		Capital Redemption Reserve	Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Retained Earnings	Total Equity
	Shares	Amount	Shares	Amount					
Balance at December 31, 2021	61,633	\$ 6	4,000	\$ 55	\$ 472	\$ 3,534,792	\$ (400,360)	\$ 830,226	\$ 3,965,191
Cumulative effect adjustment from adoption of ASU 2020-06	—	—	—	—	—	(333,524)	—	127,474	(206,050)
Issuance of ordinary shares in conjunction with exercise of share options	832	—	—	—	—	82,897	—	—	82,897
Issuance of ordinary shares under employee stock purchase plan	139	—	—	—	—	15,123	—	—	15,123
Issuance of ordinary shares in conjunction with vesting of restricted stock units	610	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(45,443)	—	—	(45,443)
Share-based compensation	—	—	—	—	—	223,279	—	—	223,279
Shares repurchased	—	—	—	—	—	—	—	(54)	(54)
Other comprehensive loss	—	—	—	—	—	—	(725,149)	—	(725,149)
Net loss	—	—	—	—	—	—	—	(224,060)	(224,060)
Balance at December 31, 2022	63,214	\$ 6	4,000	\$ 55	\$ 472	\$ 3,477,124	\$ (1,125,509)	\$ 733,586	\$ 3,085,734
Issuance of ordinary shares in conjunction with exercise of share options	280	—	—	—	—	30,189	—	—	30,189
Issuance of ordinary shares under employee stock purchase plan	156	—	—	—	—	16,270	—	—	16,270
Issuance of ordinary shares in conjunction with vesting of restricted stock units	735	—	—	—	—	—	—	—	—
Shares withheld for payment of employee's withholding tax liability	—	—	—	—	—	(50,952)	—	—	(50,952)
Share-based compensation	—	—	—	—	—	227,323	—	—	227,323
Shares repurchased	(2,130)	—	—	—	1	—	—	(269,762)	(269,761)
Other comprehensive income	—	—	—	—	—	—	283,362	—	283,362
Net income	—	—	—	—	—	—	—	414,832	414,832
Balance at December 31, 2023	62,255	\$ 6	4,000	\$ 55	\$ 473	\$ 3,699,954	\$ (842,147)	\$ 878,656	\$ 3,736,997

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JAZZ PHARMACEUTICALS PLC

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2024	2023	2022
Operating activities			
Net income (loss)	\$ 560,120	\$ 414,832	\$ (224,060)
Adjustments to reconcile net income (loss) to net cash provided by operating activities:			
Intangible asset amortization	627,313	608,284	599,169
Share-based compensation	248,045	226,841	221,996
Acquisition accounting inventory fair value step-up adjustment	135,014	151,446	273,392
Depreciation	32,754	30,412	30,302
Provision for losses on accounts receivable and inventory	27,758	11,113	14,537
Non-cash interest expense	21,973	22,378	37,973
Acquired in-process research and development	10,000	19,000	444,148
Deferred tax benefit	(208,327)	(260,217)	(292,251)
Impairment of property, plant and equipment	—	61,014	—
Intangible asset impairment charge	—	—	133,648
Loss on disposal of a business	—	—	37,704
Other non-cash transactions	17,978	11,343	(14,486)
Changes in assets and liabilities:			
Accounts receivable	(21,115)	(51,883)	(90,135)
Inventories	(45,542)	(13,420)	(49,642)
Prepaid expenses and other current assets	10,574	(126,179)	35,788
Operating lease assets	17,111	14,948	14,769
Other non-current assets	(49,820)	(15,884)	(24,038)
Accounts payable	(20,073)	9,603	(11,225)
Accrued liabilities	86,159	(23,245)	165,991
Income taxes payable	(14,742)	25,220	(1,692)
Deferred revenue	—	(463)	(2,093)
Operating lease liabilities, less current portion	(24,741)	(16,965)	(16,422)
Other non-current liabilities	(14,531)	(6,171)	(11,396)
Net cash provided by operating activities	1,395,908	1,092,007	1,271,977
Investing activities			
Acquisition of investments	(1,305,125)	(390,100)	(61,036)
Purchases of property, plant and equipment	(38,070)	(23,962)	(29,046)
Acquired in-process research and development	(10,000)	(19,000)	(444,148)
Proceeds from maturity of investments	845,000	270,000	60,000
Acquisition of intangible assets	—	—	(25,000)
Proceeds from sale of a business	—	—	53,000
Net cash used in investing activities	(508,195)	(163,062)	(446,230)
Financing activities			
Net proceeds from issuance of 2030 Notes	980,767	—	—
Proceeds from employee equity incentive and purchase plans	20,647	46,459	98,020
Payment of debt modification costs	(5,716)	—	—
Repayments of long-term debt	(31,000)	(31,000)	(582,014)
Payment of employee withholding taxes related to share-based awards	(57,753)	(50,952)	(45,443)
Share repurchases	(311,429)	(269,761)	(54)
Repayment of 2024 Notes	(575,000)	—	—
Net cash provided by (used in) financing activities	20,516	(305,254)	(529,491)
Effect of exchange rates on cash and cash equivalents	(1,675)	1,137	(6,222)
Net increase in cash and cash equivalents	906,554	624,828	290,034
Cash and cash equivalents, at beginning of period	1,506,310	881,482	591,448
Cash and cash equivalents, at end of period	\$ 2,412,864	\$ 1,506,310	\$ 881,482

JAZZ PHARMACEUTICALS PLC
CONSOLIDATED STATEMENTS OF CASH FLOWS—(Continued)
(In thousands)

	Year Ended December 31,		
	2024	2023	2022
Supplemental disclosure of cash flow information:			
Cash paid for interest	\$ 314,822	\$ 333,112	\$ 270,671
Cash paid for income taxes, net of refunds	114,907	177,880	94,681

The accompanying notes are an integral part of these consolidated financial statements.

JAZZ PHARMACEUTICALS PLC

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Organization and Description of Business

Jazz Pharmaceuticals plc is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases - often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines, including leading therapies for sleep disorders and epilepsy, and a growing portfolio of cancer treatments. Our patient-focused and science-driven approach powers pioneering research and development advancements across our robust pipeline of innovative therapeutics in oncology and neuroscience.

Our lead marketed products, listed below, are approved in countries around the world to improve patient care.

Neuroscience

- **Xywav® (calcium, magnesium, potassium, and sodium oxybates) oral solution**, a product approved by FDA in July 2020, and launched in the U.S. in November 2020 for the treatment of cataplexy or EDS in patients seven years of age and older with narcolepsy, and also approved by FDA in August 2021 for the treatment of IH in adults and launched in the U.S. in November 2021. Xywav contains 92% less sodium than Xyrem®. Xywav is also approved in Canada for the treatment of cataplexy in patients with narcolepsy.
- **Epidiolex® (cannabidiol) oral solution**, a product approved by FDA and launched in the U.S. in 2018 by GW and currently indicated for the treatment of seizures associated with LGS, DS, or TSC in patients one year of age or older; in the EU and Great Britain (where it is marketed as Epidyolex®) and other markets, it is approved for adjunctive treatment of seizures associated with LGS or DS, in conjunction with clobazam (EU and Great Britain only), in patients 2 years of age and older and for adjunctive treatment of seizures associated with TSC in patients 2 years of age and older.

Oncology

- **Rylaze® (asparaginase erwinia chrysanthemi (recombinant)-rywn)**, a product approved by FDA in June 2021 and launched in the U.S. in July 2021 for use as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL or LBL in adults and pediatric patients aged one month or older who have developed hypersensitivity to *E. coli*-derived asparaginase. In September 2023, the European Commission granted marketing authorization under the trade name Enrylaze. This therapy is also approved in markets including Great Britain, Canada and Switzerland.
- **Zepzelca® (lurbinectedin)**, a product approved by FDA in June 2020 under FDA's accelerated approval pathway and launched in the U.S. in July 2020 for the treatment of adult patients with metastatic SCLC with disease progression on or after platinum-based chemotherapy; in Canada, Zepzelca received conditional approval in September 2021 for the treatment of adults with Stage III or metastatic SCLC, who have progressed on or after platinum-containing therapy.
- **Ziihera® (zanidatamab-hrii)**, a product approved by FDA in November 2024 under FDA's accelerated approval pathway and launched in the U.S. in December 2024 for the treatment of adults with previously treated, unresectable or metastatic HER2-positive (IHC 3+) BTC, as detected by an FDA-approved test.

Throughout this report, unless otherwise indicated or the context otherwise requires, all references to "Jazz Pharmaceuticals," "the registrant," "the Company", "we," "us," and "our" refer to Jazz Pharmaceuticals plc and its consolidated subsidiaries. Throughout this report, all references to "ordinary shares" refer to Jazz Pharmaceuticals plc's ordinary shares.

2. Summary of Significant Accounting Policies***Basis of Presentation***

The consolidated financial statements have been prepared in accordance with U.S. GAAP, and include the accounts of Jazz Pharmaceuticals plc and our subsidiaries. Intercompany transactions and balances have been eliminated. Our consolidated financial statements include the results of operations of businesses we have acquired from the date of each acquisition for the applicable reporting periods.

Use of Estimates

The preparation of financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses, and related disclosures in the consolidated financial statements and accompanying notes. Management bases its estimates on historical experience and on assumptions believed to be reasonable under the circumstances. Actual results could differ materially from those estimates.

Adoption of New Accounting Standards

In November 2023, the FASB issued ASU 2023-07, “Segment Reporting (Topic 280) - Improvements to Reportable Segment Disclosures”, which requires enhanced disclosures about significant segment expenses. The amendments are effective retrospectively to all prior periods presented in the financial statements, for fiscal years beginning after December 15, 2023. The new guidance has not had a material impact on our financial statement disclosures.

Significant Risks and Uncertainties

We expect that our business will continue to meaningfully depend on oxybate revenues; however, there is no guarantee that oxybate revenues will remain at current levels. In this regard, our ability to maintain oxybate revenues and realize the anticipated benefits from our investment in Xywav are subject to a number of risks and uncertainties including, without limitation, those related to the commercialization of Xywav for the treatment of IH in adults and adoption in that indication; competition from the introduction of two AG versions of high-sodium oxybate and a branded fixed-dose, high-sodium oxybate, Avadel's Lumryz, for treatment of cataplexy and/or EDS in narcolepsy in the U.S. market, as well as potential future competition from additional AG versions of high-sodium oxybate and from generic versions of high-sodium oxybate and from other competitors; increased pricing pressure from, changes in policies by, or restrictions on reimbursement imposed by, third party payors, including our ability to maintain adequate coverage and reimbursement for Xywav; increased rebates required to maintain access to our products; challenges to our intellectual property around Xywav and/or Xyrem, including from pending antitrust and intellectual property litigation; and continued acceptance of Xywav and Xyrem by physicians and patients. A significant decline in oxybate revenues could cause us to reduce our operating expenses or seek to raise additional funds and would have a material adverse effect on our business, financial condition, results of operations and growth prospects, including on our ability to acquire, in-license or develop new products to grow our business.

In addition to risks related specifically to Xywav and Xyrem, we are subject to other challenges and risks related to successfully commercializing a portfolio of oncology products and other neuroscience products, and other risks specific to our business and our ability to execute on our strategy, as well as risks and uncertainties common to companies in the pharmaceutical industry with development and commercial operations, including, without limitation, risks and uncertainties associated with: ongoing clinical research activity and related outcomes; obtaining regulatory approval of our late-stage product candidates; effectively commercializing our approved products such as Epidiolex, Rylaze, Zepzelca and Ziihera; obtaining and maintaining adequate coverage and reimbursement for our products; contracting and rebates to pharmacy benefit managers and similar organizations that reduce our net revenue; increasing scrutiny of pharmaceutical product pricing and resulting changes in healthcare laws and policy; market acceptance; regulatory concerns with controlled substances generally and the potential for abuse; future legislation; action by the U.S. Federal Government authorizing the sale, distribution, use, and insurance reimbursement of non-FDA approved cannabinoid products; delays or problems in the supply of our products; loss of single source suppliers or failure to comply with manufacturing regulations; delays or problems with third parties that are part of our manufacturing and supply chain; identifying, acquiring or in-licensing additional products or product candidates; our ability to realize the anticipated benefits of acquired or in-licensed products or product candidates, such as Epidiolex and Ziihera, at the expected levels, with the expected costs and within the expected timeframe; pharmaceutical product development and the inherent uncertainty of clinical success; the challenges of protecting and enhancing our intellectual property rights; complying with applicable regulatory requirements; and possible restrictions on our ability and flexibility to pursue certain future opportunities as a result of our substantial outstanding debt obligations.

Concentrations of Risk

Financial instruments that potentially subject us to concentrations of credit risk consist of cash, cash equivalents, investments and derivative contracts. Our investment policy permits investments in U.S. federal government and federal agency securities, corporate bonds or commercial paper issued by U.S. corporations, money market instruments, certain qualifying money market mutual funds, certain repurchase agreements, and tax-exempt obligations of U.S. states, agencies and municipalities and places restrictions on credit ratings, maturities, and concentration by type and issuer. We are exposed to credit risk in the event of a default by the financial institutions holding our cash, cash equivalents and investments to the extent recorded on the balance sheet.

We manage our foreign currency transaction risk and interest rate risk within specified guidelines through the use of derivatives. All of our derivative instruments are utilized for risk management purposes, and we do not use derivatives for speculative trading purposes. As of December 31, 2024 and 2023, we had foreign exchange forward contracts with notional amounts totaling \$461.2 million and \$511.7 million, respectively. As of December 31, 2024 and 2023, the outstanding foreign exchange forward contracts had a net liability fair value of \$7.9 million and a net asset fair value of \$17.4 million, respectively. As of December 31, 2024 and 2023, we had interest rate swap contracts with notional amounts totaling \$500.0 million. As of December 31, 2024 and 2023, these outstanding interest rate swap contracts had a net asset fair value of \$1.0 million and \$0.4 million, respectively. The counterparties to these contracts are large multinational commercial banks, and we believe the risk of nonperformance is not significant.

We are also subject to credit risk from our accounts receivable related to our product sales. We monitor our exposure within accounts receivable and record a reserve against uncollectible accounts receivable as necessary. We extend credit to pharmaceutical wholesale distributors and specialty pharmaceutical distribution companies, primarily in the U.S., and to other international distributors and hospitals. Customer creditworthiness is monitored and collateral is not required. We monitor economic conditions in certain European countries which may result in variability of the timing of cash receipts and an increase in the average length of time that it takes to collect accounts receivable outstanding. Historically, we have not experienced significant credit losses on our accounts receivable and as of December 31, 2024, allowances on receivables were not material. As of December 31, 2024, five customers accounted for 80% of gross accounts receivable, including ESSDS, which accounted for 39% of gross accounts receivable, ASD, which accounted for 15% of gross accounts receivable and McKesson, which accounted for 13% of gross accounts receivable. As of December 31, 2023, five customers accounted for 79% of gross accounts receivable, including ESSDS, which accounted for 41% of gross accounts receivable, ASD, which accounted for 13% of gross accounts receivable and McKesson, which accounted for 11% of gross accounts receivable.

We depend on single source suppliers for most of our products, product candidates and their APIs. With respect to our oxybate products, the API is manufactured for us by a single source supplier and the finished products are manufactured both by us in our facility in Athlone, Ireland and by our U.S.-based supplier.

Business Acquisitions

Our consolidated financial statements include the results of operations of an acquired business from the date of acquisition. We account for acquired businesses using the acquisition method of accounting. The acquisition method of accounting for acquired businesses requires, among other things, that assets acquired, liabilities assumed and any noncontrolling interests in the acquired business be recognized at their estimated fair values as of the acquisition date, with limited exceptions, and that the fair value of acquired IPR&D, be recorded on the balance sheet. Also, transaction costs are expensed as incurred. Any excess of the acquisition consideration over the assigned values of the net assets acquired is recorded as goodwill. Contingent consideration is included within the acquisition cost and is recognized at its fair value on the acquisition date. A liability resulting from contingent consideration is remeasured to fair value at each reporting date until the contingency is resolved and changes in fair value are recognized in earnings.

Cash Equivalents and Investments

We consider all highly liquid investments, readily convertible to cash, that mature within three months or less from date of purchase to be cash equivalents.

Investments consist of time deposits with initial maturities of greater than three months. Collectively, cash equivalents and investments are considered available-for-sale and are recorded at fair value. Unrealized gains and losses, net of tax, are recorded in accumulated other comprehensive loss in shareholders' equity. We use the specific-identification method for calculating realized gains and losses on securities sold. Realized gains and losses and declines in value judged to be other than temporary on investments are included in interest expense, net in the consolidated statements of income (loss).

Derivative Instruments and Hedging Activities

We record the fair value of derivative instruments as either assets or liabilities on the consolidated balance sheets. Changes in the fair value of derivative instruments are recorded each period in current earnings or other comprehensive income (loss), depending on whether a derivative instrument is designated as part of a hedging transaction and, if it is, the type of hedging transaction. For a derivative to qualify as a hedge at inception and throughout the hedged period, we formally document the nature and relationships between the hedging instruments and hedged item.

For derivatives formally designated as hedges, we assess both at inception and quarterly thereafter, whether the hedging derivatives are highly effective in offsetting changes in either the fair value or cash flows of the hedged item.

Gains or losses on cash flow hedges are reclassified from other comprehensive income (loss) to earnings when the hedged transaction occurs. If we determine that a forecasted transaction is no longer probable of occurring, we discontinue hedge accounting and any related unrealized gain or loss on the derivative instrument is recognized in current earnings.

We designate cross-currency interest rate swaps as fair value hedges to hedge foreign currency risks related to our borrowings denominated in currencies other than the U.S. dollar. Fair value hedge amounts included in the assessment of hedge effectiveness are recognized in foreign exchange gain (loss) within the consolidated statements of income (loss), along with the offsetting gains and losses of the related hedged item. We have elected to exclude the total forward points or currency basis from the assessment of hedge effectiveness and account for them as excluded components. The initial fair value of the excluded component is amortized to foreign exchange gain (loss) and the difference between changes in fair value of the excluded component and the amount recorded in earnings is recorded in other comprehensive income (loss).

Derivatives that are not designated and do not qualify as hedges are adjusted to fair value through current earnings.

Inventories

Inventories are valued at the lower of cost or net realizable value. Cost is determined using the first-in, first-out method for all inventories. Our policy is to write down inventory that has become obsolete, inventory that has a cost basis in excess of its expected net realizable value and inventory in excess of expected requirements. The estimate of excess quantities is subjective and primarily dependent on our estimates of future demand for a particular product. If our estimate of future demand changes, we consider the impact on the reserve for excess inventory and adjust the reserve as required. Increases in the reserve are recorded as charges in cost of product sales.

We capitalize inventory costs associated with our products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The determination to capitalize inventory costs is based on various factors, including status and expectations of the regulatory approval process, any known safety or efficacy concerns, potential labeling restrictions, and any other impediments to obtaining regulatory approval. We had no pre-approval inventory on our consolidated balance sheet as of December 31, 2024 or 2023.

Our inventory production process for our cannabinoid products includes the cultivation of botanical raw material. Because of the duration of the cultivation process, a portion of our inventory will not be sold within one year. Consistent with the practice in other industries that cultivate botanical raw materials, all inventory is classified as a current asset.

Property, Plant and Equipment

Property, plant and equipment are stated at cost, less accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Estimated useful lives are as follows:

Buildings	40 years
Manufacturing equipment and machinery	4-20 years
Computer software and equipment	3-7 years
Furniture and fixtures	5 years

Leasehold improvements are amortized over the shorter of the noncancelable term of our leases or their economic useful lives. Maintenance and repairs are expensed as incurred.

Leases

We determine if an arrangement is a lease at inception. Leases are classified at lease commencement as either operating leases or finance leases. Operating leases are included in operating lease assets, accrued liabilities, and operating lease liabilities on our consolidated balance sheets. Finance lease assets are included in property, plant and equipment, net, and finance lease liabilities are included in accrued liabilities and other non-current liabilities in our consolidated balance sheets. Lease assets and lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. In determining the net present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. The lease asset also includes any lease payments made, reduced by lease incentives and increased by initial direct costs incurred. Our lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Operating lease expense for minimum lease payments is recognized on a straight-line basis over the lease term. Finance lease expense is recognized as depreciation expense of property, plant and equipment and interest expense on finance lease liabilities.

We have lease agreements with lease and non-lease components, which are generally accounted for separately. For vehicle leases we account for the lease and non-lease components as a single lease component.

We have elected the short-term lease exemption and, therefore, do not recognize a lease asset or corresponding liability for lease arrangements with an original term of 12 months or less. Rent expense under short-term leases is recognized on a straight-line basis over the lease term.

Goodwill

Goodwill represents the excess of the acquisition consideration over the fair value of assets acquired and liabilities assumed. We have determined that we operate in a single segment and have a single reporting unit associated with the development and commercialization of pharmaceutical products. In performing the annual impairment test, the fair value of the reporting unit is compared to its corresponding carrying value, including goodwill. If the carrying value exceeds the fair value of the reporting unit an impairment loss will be recognized for the amount by which the reporting unit's carrying amount exceeds its fair value, not to exceed the carrying amount of goodwill. We test goodwill for impairment annually in October and when events or changes in circumstances indicate that the carrying value may not be recoverable.

Acquired In-Process Research and Development

The initial costs of rights to IPR&D projects acquired in an asset acquisition are expensed as IPR&D unless the project has an alternative future use. The fair value of IPR&D projects acquired in a business combination are capitalized and accounted for as indefinite-lived intangible assets until the underlying project receives regulatory approval, at which point the intangible asset will be accounted for as a finite-lived intangible asset, or discontinued, at which point the intangible asset will be written off. Development costs incurred after an acquisition are expensed as incurred.

Intangible Assets

Intangible assets with finite useful lives consist primarily of purchased developed technology and are amortized on a straight-line basis over their estimated useful lives, which range from seven to sixteen years. The estimated useful lives associated with finite-lived intangible assets are consistent with the estimated lives of the associated products and may be modified when circumstances warrant. Such assets are reviewed for impairment when events or circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of an asset and its eventual disposition are less than its carrying amount. The amount of any impairment is measured as the difference between the carrying amount and the fair value of the impaired asset.

Revenue Recognition

Our revenue is comprised of product sales, net and royalties and contract revenues. Revenues are recognized when control of the promised goods or services is transferred to our customers, in an amount that reflects the consideration we expect to be entitled to in exchange for those goods or services. Prior to recognizing revenue, we make estimates of the transaction price, including variable consideration that is subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved.

Product Sales, Net

Product sales revenue is recognized when control has transferred to the customer, which occurs at a point in time, which is typically on delivery to the customer or, in the case of products that are subject to consignment agreements, when the customer removes product from our consigned inventory location for shipment directly to a patient.

Reserves for Variable Consideration

Revenues from sales of products are recorded at the net sales price, which includes estimates of variable consideration for which reserves are established and which relate to returns, specialty distributor fees, wholesaler fees, prompt payment discounts, government rebates, government chargebacks, coupon programs and rebates under managed care plans and commercial payor contracts. Calculating certain of these reserves involves estimates and judgments and we determine their expected value based on sales or invoice data, contractual terms, historical utilization rates, new information regarding changes in these programs' regulations and guidelines that would impact the amount of the actual rebates, our expectations regarding future utilization rates for these programs and channel inventory data. These reserves reflect our best estimates of the amount of consideration to which we are entitled based on the terms of the contract. A large portion of the reserve relates to rebates where there is significant judgment, in particular in the determination of the sales utilization percentage used to calculate the Epidiolex Medicaid rebate accrual. The amount of variable consideration that is included in the transaction price may be constrained, and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of

the cumulative revenue recognized will not occur in a future period. We reassess our reserves for variable consideration at each reporting date. Historically, adjustments to estimates for these reserves have not been material.

Reserves for returns, specialty distributor fees, wholesaler fees, government rebates, coupon programs and rebates under managed care plans and commercial payor contracts are included within current liabilities in our consolidated balance sheets. Reserves for government chargebacks and prompt payment discounts are shown as a reduction in accounts receivable.

Royalties and Contract Revenues

We enter into out-licensing agreements under which we license certain rights to our products or product candidates to third parties. If a licensing arrangement includes multiple goods or services, we consider whether the license is distinct. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, upfront fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. If the license to our intellectual property is determined not to be distinct, it is combined with other goods or services into a combined performance obligation. We consider whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. We evaluate the measure of progress each reporting date and, if necessary, adjust the measure of performance and related revenue recognition.

At the inception of each arrangement that includes development milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or that of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability of achievement of such development milestones and any related constraint, and if necessary, adjust our estimate of the overall transaction price.

For arrangements that include sales-based royalties and milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties and sales-based milestones relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty or sales-based milestone has been allocated has been satisfied (or partially satisfied).

Cost of Product Sales

Cost of product sales includes manufacturing and distribution costs, the cost of drug substance, royalties due to third parties on product sales, product liability and cargo insurance, FDA user fees, freight, shipping, handling and storage costs and salaries and related costs of employees involved with production. Excluded from cost of product sales shown on the consolidated statements of income (loss) is amortization of acquired developed technology of \$627.3 million, \$608.3 million and \$599.2 million in 2024, 2023 and 2022, respectively.

Research and Development

Research and development expenses consist primarily of costs related to clinical studies and outside services, personnel expenses, and other research and development costs, including milestone payments incurred prior to regulatory approval of products. Clinical study and outside services costs relate primarily to services performed by clinical research organizations, clinical studies performed at clinical sites, materials and supplies, and other third party fees. Personnel expenses relate primarily to salaries, benefits and share-based compensation. Other research and development expenses primarily include overhead allocations consisting of various support and facilities-related costs. Research and development costs are expensed as incurred. For product candidates that have not been approved by FDA, inventory used in clinical trials is expensed at the time of production and recorded as research and development expense. For products that have been approved by FDA, inventory used in clinical trials is expensed at the time the inventory is packaged for the trial.

Advertising Expenses

We expense the costs of advertising, including promotional expenses, as incurred. Advertising expenses were \$107.4 million, \$92.2 million and \$108.8 million in 2024, 2023 and 2022, respectively.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial statement carrying amount and the tax basis of assets and

liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided to reduce deferred tax assets to the amount that is more-likely-than-not to be realized. We recognize the benefits of a tax position if it is more-likely-than-not of being sustained. A recognized tax benefit is then measured as the largest amount of tax benefit that is greater than fifty percent likely of being realized upon settlement. Interest and penalties related to income taxes are included in income tax expense and classified with the related liability on the consolidated balance sheets.

Foreign Currency

Our functional and reporting currency is the U.S. dollar. The assets and liabilities of our subsidiaries that have a functional currency other than the U.S. dollar are translated into U.S. dollars at the exchange rate prevailing at the balance sheet date with the results of operations of subsidiaries translated at the weighted average exchange rate for the reporting period. The cumulative foreign currency translation adjustment is recorded as a component of accumulated other comprehensive income (loss) in shareholders' equity.

Transactions in foreign currencies are translated into the functional currency of the relevant subsidiary at the weighted average exchange rate for the reporting period. Any monetary assets and liabilities arising from these transactions are translated into the relevant functional currency at exchange rates prevailing at the balance sheet date or on settlement. Resulting gains and losses are recorded in foreign exchange gain (loss) in our consolidated statements of income (loss).

Deferred Financing Costs

Deferred financing costs are reported at cost, less accumulated amortization and are presented in the consolidated balance sheets as a direct deduction from the carrying value of the associated debt, with the exception of deferred financing costs associated with revolving-debt arrangements which are presented as assets. The related amortization expense is included in interest expense, net in our consolidated statements of income (loss).

Contingencies

From time to time, we may become involved in claims and other legal matters arising in the ordinary course of business. We record accruals for loss contingencies to the extent that we conclude that it is probable that a liability has been incurred and the amount of the related loss can be reasonably estimated. Legal fees and other expenses related to litigation are expensed as incurred and included in selling, general and administrative expenses.

Share-Based Compensation

We account for compensation cost for all share-based awards at fair value on the date of grant. The fair value is recognized as expense over the service period, net of estimated forfeitures, using the straight-line method. The estimation of share-based awards that will ultimately vest requires judgment, and, to the extent actual results or updated estimates differ from current estimates, such amounts will be recorded as a cumulative adjustment in the period estimates are revised. We primarily consider historical experience when estimating expected forfeitures.

Performance-Based Restricted Stock Unit Awards

PRSUs awarded to employees vest upon the achievement of certain performance criteria at the end of a specified performance period. For PRSUs granted prior to 2024, the amount of shares awarded will be subject to adjustment based on the application of a TSR modifier. For PRSUs granted in 2024, the relative TSR modifier represents one of the performance metrics. The estimated fair value of these PRSUs is based on a Monte Carlo simulation model. Compensation expense for PRSUs is recognized from the date the Company determines the performance criteria probable of being achieved to the date the award, or relevant portion of the award, is expected to vest. Cumulative adjustments are recorded on a quarterly basis to reflect subsequent changes to the estimated outcome of the performance criteria until the date results are determined.

Variable Interest Entity

In 2021, we invested in a protected cell as part of our directors' and officers' liability risk financing strategy. Based on our control and the structure of the protected cell, we concluded that Jazz is the primary beneficiary of the protected cell and is required to consolidate the protected cell. There was no insurance premium payable to the protected cell for the years ended December 31, 2024 and 2023 and it was immaterial for the year ended December 31, 2022. The protected cell's assets and liabilities as of December 31, 2024 and 2023 were immaterial.

Recent Accounting Pronouncements

In December 2023, the FASB issued ASU 2023-09, "Income Taxes (Topic 740) - Improvements to Income Tax Disclosures", which requires enhanced income tax disclosures providing greater disaggregation of information in the

Company's effective tax rate reconciliation and disaggregates income taxes paid by jurisdiction. The amendments are effective on a prospective basis, with the option to apply it retrospectively, for fiscal years beginning after December 15, 2024. We are currently evaluating the impact of adopting this new accounting guidance.

In November 2024, the FASB issued ASU 2024-03, "Income Statement - Reporting Comprehensive Income - Expense Disaggregation Disclosures (Subtopic 220-04) - Disaggregation of Income Statement Expenses", which requires additional disclosure in the notes to the financial statements of the nature of certain expenses included in the income statement. The amendments are effective on a prospective basis, with the option to apply it retrospectively, for fiscal years beginning after December 15, 2026. We are currently evaluating the impact of adopting this new accounting guidance.

3. Collaborations and Disposition

License Agreements

In February 2024, we entered into a definitive asset purchase agreement with Redx to acquire global rights to a KRAS inhibitor program. Under the terms of the agreement, we made an upfront payment of \$10.0 million to Redx which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2024. Redx is eligible to receive development and commercial milestone payments of up to \$870.0 million and, if a product is approved, a tiered, mid-single-digit percentage royalty on net sales of that product.

In November 2023, we entered into an exclusive licensing and collaboration agreement with Autifony to discover and develop drug candidates targeting two different ion channel targets associated with neurological disorders. Under the terms of the agreement, we made an upfront payment of \$18.0 million to Autifony, which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2023. Autifony is eligible to receive development and commercial milestone payments of up to \$752.5 million and, if a product is approved, a tiered, mid-single-digit percentage royalty on net sales of that product.

In October 2022, we entered into an exclusive licensing and collaboration agreement with Zymeworks providing us the right to acquire development and commercialization rights to Zymeworks' zanidatamab across all indications in the United States, Europe, Japan and all other territories except for those Asia/Pacific territories previously licensed by Zymeworks. In December 2022, we exercised the option to continue with the exclusive development and commercialization rights to zanidatamab. Zanidatamab is a bispecific antibody that can simultaneously bind two non-overlapping epitopes of HER2, known as biparatopic binding. Under the terms of the agreement, Zymeworks received an upfront payment of \$50.0 million and, following our decision to continue the collaboration after the readout of the top-line clinical data from HERIZON-BTC-01, a second, one-time payment of \$325.0 million. We recorded the \$375.0 million as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022. In November 2024, we announced FDA accelerated approval of Ziihera for the treatment of adults with previously treated, unresectable or metastatic HER2-positive biliary tract cancer, triggering a regulatory milestone payment of \$25.0 million, which was capitalized as an intangible asset on our consolidated balance sheet. Zymeworks is also eligible to receive regulatory and commercial milestone payments of up to \$1.4 billion, for total potential payments of \$1.8 billion, as well as incremental tiered royalties on future net sales of Ziihera ranging from 10% to 20%.

In May 2022, we entered into a licensing agreement with Sumitomo to acquire exclusive development and commercialization rights in the U.S., Europe and other territories for DSP-0187, now referred to as JZP441. JZP441 is a potent, highly selective oral orexin-2 receptor agonist with potential application for the treatment of narcolepsy, IH and other sleep disorders. Under the terms of the agreement, we made an upfront payment of \$50.0 million to Sumitomo, which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022. Sumitomo is eligible to receive development, regulatory and commercial milestone payments of up to \$1.09 billion and, if JZP441 is approved, a tiered, low double-digit royalty on Jazz's net sales of JZP441.

In April 2022, we entered into a licensing and collaboration agreement with Werewolf to acquire exclusive global development and commercialization rights to Werewolf's investigational WTX-613, now referred to as JZP898. JZP898 is a differentiated, conditionally-activated interferon alpha (IFN α) INDUKINE™ molecule. We made an upfront payment of \$15.0 million to Werewolf in 2022, which was recorded as acquired IPR&D expense in our consolidated statements of income (loss) for the year ended December 31, 2022, and a milestone payment of \$5.0 million in September 2023 which was recorded within research and development expense in our consolidated statements of income (loss) for the year ended December 31, 2023. Werewolf is eligible to receive further development, regulatory and commercial milestone payments of up to \$1.26 billion and, if JZP898 is approved, a tiered, mid-single-digit percentage royalty on net sales of JZP898.

Sunosi Disposition

In March 2022, we entered into a definitive agreement to divest Sunosi to Axsome. In May 2022, we completed the U.S. divestiture and in November 2022, the ex-U.S. divestiture was completed. Under the terms of the sale agreement, Axsome received the rights to Sunosi in all of the existing territories available to us. We received an upfront payment of \$53.0 million, and have the right to receive a high single-digit royalty on Axsome's U.S. net sales of Sunosi in current indications and a mid-single-digit royalty on Axsome's U.S. net sales of Sunosi in future indications.

Upon closing, we recognized a loss on disposal of \$40.8 million within selling, general and administrative expenses in our consolidated statements of income (loss) in the year ended December 31, 2022. We are accounting for the contingent consideration in the form of the future royalty as it is earned.

We determined that the disposal of Sunosi did not qualify for reporting as a discontinued operation since it did not represent a strategic shift that has or will have a major effect on our operations and financial results.

4. Cash and Available-for-Sale Securities

Cash, cash equivalents and investments consisted of the following (in thousands):

	December 31, 2024					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	\$ 948,894	\$ —	\$ —	\$ 948,894	\$ 948,894	\$ —
Time deposits	790,000	—	—	790,000	210,000	580,000
Money market funds	1,253,970	—	—	1,253,970	1,253,970	—
Totals	<u>\$ 2,992,864</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 2,992,864</u>	<u>\$ 2,412,864</u>	<u>\$ 580,000</u>

	December 31, 2023					
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value	Cash and Cash Equivalents	Investments
Cash	\$ 437,724	\$ —	\$ —	\$ 437,724	\$ 437,724	\$ —
Time deposits	420,000	—	—	420,000	300,000	120,000
Money market funds	768,586	—	—	768,586	768,586	—
Totals	<u>\$ 1,626,310</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 1,626,310</u>	<u>\$ 1,506,310</u>	<u>\$ 120,000</u>

Cash equivalents and investments are considered available-for-sale securities. We use the specific-identification method for calculating realized gains and losses on securities sold and include them in interest expense, net in the consolidated statements of income (loss). Our investment balances represent time deposits with original maturities of greater than three months and less than one year. Interest income from available-for-sale securities was \$106.3 million, \$65.1 million and \$11.5 million in 2024, 2023 and 2022, respectively.

5. Fair Value Measurement

The following table summarizes, by major security type, our available-for-sale securities and derivative contracts that were measured at fair value on a recurring basis and were categorized using the fair value hierarchy (in thousands):

	December 31, 2024			December 31, 2023		
	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Total Estimated Fair Value
Assets:						
Available-for-sale securities:						
Money market funds	\$ 1,253,970	\$ —	\$ 1,253,970	\$ 768,586	\$ —	\$ 768,586
Time deposits	—	790,000	790,000	—	420,000	420,000
Foreign exchange forward contracts	—	2,250	2,250	—	18,035	18,035
Interest rate contracts	—	991	991	—	3,784	3,784
Totals	<u>\$ 1,253,970</u>	<u>\$ 793,241</u>	<u>\$ 2,047,211</u>	<u>\$ 768,586</u>	<u>\$ 441,819</u>	<u>\$ 1,210,405</u>
Liabilities:						
Foreign exchange forward contracts	\$ —	\$ 10,198	\$ 10,198	\$ —	\$ 681	\$ 681
Interest rate contracts	—	—	—	—	3,410	3,410
Totals	<u>\$ —</u>	<u>\$ 10,198</u>	<u>\$ 10,198</u>	<u>\$ —</u>	<u>\$ 4,091</u>	<u>\$ 4,091</u>

As of December 31, 2024 and 2023, our available-for-sale securities included money market funds and time deposits and their carrying values were approximately equal to their fair values. Money market funds were measured using quoted prices in active markets, which represent Level 1 inputs and time deposits were measured at fair value using Level 2 inputs. Level 2 inputs are obtained from various third party data providers and represent quoted prices for similar assets in active markets, or these inputs were derived from observable market data, or if not directly observable, were derived from or corroborated by other observable market data.

Our derivative assets and liabilities include interest rate and foreign exchange derivatives that are measured at fair value using observable market inputs such as forward rates, interest rates, our own credit risk as well as an evaluation of our counterparties' credit risks. Based on these inputs, the derivative assets and liabilities are classified within Level 2 of the fair value hierarchy.

There were no transfers between the different levels of the fair value hierarchy in 2024 or in 2023.

As of December 31, 2024 and 2023, the carrying amount of investments measured using the measurement alternative for equity investments without a readily determinable fair value was \$4.3 million and \$4.7 million, respectively. The carrying amount, which is recorded within other non-current assets, is based on the latest observable transaction price.

As of December 31, 2024, the estimated fair values of the 2026 Notes, the 2030 Notes, the Secured Notes and the Tranche B-2 Dollar Term Loans were \$1.0 billion, \$1.1 billion, \$1.4 billion and \$2.7 billion, respectively. The fair values of each of these debt facilities was estimated using quoted market prices obtained from brokers (Level 2).

6. Derivative Instruments and Hedging Activities

We are exposed to certain risks arising from operating internationally, including fluctuations in foreign exchange rates primarily related to the translation of sterling and euro denominated net monetary liabilities, including intercompany balances, held by subsidiaries with a U.S. dollar functional currency and fluctuations in interest rates on our outstanding term loan borrowings. We manage these exposures within specified guidelines through the use of derivatives. All of our derivative instruments are utilized for risk management purposes, and we do not use derivatives for speculative trading purposes.

We enter into foreign exchange forward contracts, with durations of up to 12 months, designed to limit the exposure to fluctuations in foreign exchange rates related to the translation of certain non-U.S. dollar denominated liabilities, including intercompany balances. Hedge accounting is not applied to these derivative instruments as gains and losses on these hedge transactions are designed to offset gains and losses on underlying balance sheet exposures. As of December 31, 2024 and 2023,

the notional amount of foreign exchange contracts where hedge accounting was not applied was \$461.2 million and \$511.7 million, respectively.

The foreign exchange gain (loss) in our consolidated statements of income (loss) included the following gains (losses) associated with foreign exchange contracts not designated as hedging instruments (in thousands):

Foreign Exchange Forward Contracts:	Year Ended December 31,		
	2024	2023	2022
Gain (loss) recognized in foreign exchange gain (loss)	\$ (14,444)	\$ 13,543	\$ (58,755)

To achieve a desired mix of floating and fixed interest rates on our variable rate debt, we entered into interest rate swap agreements in April 2023 which are effective until April 2026. These agreements hedge contractual term loan interest rates. As of December 31, 2024, the interest rate swap agreements had a notional amount of \$500.0 million. As a result of these agreements, the interest rate on a portion of our term loan borrowings is fixed at 3.9086%, plus the borrowing spread, until April 30, 2026.

The impact on accumulated other comprehensive loss and earnings from derivative instruments that qualified as cash flow hedges was as follows (in thousands):

Interest Rate Contracts:	Year Ended December 31,	
	2024	2023
Gain recognized in accumulated other comprehensive loss, net of tax	\$ 5,298	\$ 3,658
Gain reclassified from accumulated other comprehensive loss to interest expense, net of tax	(4,793)	(3,423)

Assuming no change in the Term SOFR based interest rates from market rates as of December 31, 2024, \$0.7 million of gains, net of tax, recognized in accumulated other comprehensive loss will be reclassified to earnings over the next 12 months.

In order to hedge our exposure to foreign currency exchange risk associated with our Euro Term Loan, we entered into a cross-currency interest rate swap contract in May 2021, which matured in March 2022, and was de-designated as a fair value hedge. The terms of this contract converted the principal repayments and interest payments on the Euro Term Loan into U.S. dollars. The carrying amount of the Euro Term Loan and the fair value of the cross-currency interest rate swap contract were remeasured on a monthly basis, with changes in the euro to U.S. dollar foreign exchange rates recognized within foreign exchange gain (loss) in the consolidated statements of income (loss).

The impact on accumulated other comprehensive loss and earnings from the cross-currency interest rate swap contract was as follows (in thousands):

Cross-Currency Interest Rate Contract:	Year Ended December 31,	
	2022	
Loss reclassified from accumulated other comprehensive loss to foreign exchange loss, net of tax	\$	128
Loss recognized in foreign exchange loss		2,646

The cash flow effects of our derivative contracts are included within net cash provided by operating activities in the consolidated statements of cash flows, except for the settlement of notional amounts of the cross-currency swap, which were included in net cash used in financing activities.

The following tables summarize the fair value of outstanding derivatives (in thousands):

December 31, 2024				
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	Fair Value	Balance Sheet Location	Fair Value
Derivatives designated as hedging instruments:				
Interest rate contracts	Other current assets	\$ 959	Accrued liabilities	\$ —
	Other non-current assets	32	Other non-current liabilities	—
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	2,250	Accrued liabilities	10,198
Total fair value of derivative instruments		<u>\$ 3,241</u>		<u>\$ 10,198</u>
December 31, 2023				
	Asset Derivatives		Liability Derivatives	
	Balance Sheet Location	Fair Value	Balance Sheet Location	Fair Value
Derivatives designated as hedging instruments:				
Interest rate contracts	Other current assets	\$ 3,784	Accrued liabilities	\$ —
	Other non-current assets	—	Other non-current liabilities	3,410
Derivatives not designated as hedging instruments:				
Foreign exchange forward contracts	Other current assets	18,035	Accrued liabilities	681
Total fair value of derivative instruments		<u>\$ 21,819</u>		<u>\$ 4,091</u>

Although we do not offset derivative assets and liabilities within our consolidated balance sheets, our International Swap and Derivatives Association agreements provide for net settlement of transactions that are due to or from the same counterparty upon early termination of the agreement due to an event of default or other termination event. The following table summarizes the potential effect on our consolidated balance sheets of offsetting our interest rate and foreign exchange forward contracts subject to such provisions (in thousands):

December 31, 2024						
Description	Gross Amounts of Recognized Assets/ Liabilities	Gross Amounts Offset in the Consolidated Balance Sheet	Net Amounts of Assets/ Liabilities Presented in the Consolidated Balance Sheet	Gross Amounts Not Offset in the Consolidated Balance Sheet		
				Derivative Financial Instruments	Cash Collateral Received (Pledged)	Net Amount
Derivative assets	\$ 3,241	\$ —	\$ 3,241	\$ (2,910)	\$ —	\$ 331
Derivative liabilities	(10,198)	—	(10,198)	2,910	—	(7,288)
December 31, 2023						
Description	Gross Amounts of Recognized Assets/ Liabilities	Gross Amounts Offset in the Consolidated Balance Sheet	Net Amounts of Assets/ Liabilities Presented in the Consolidated Balance Sheet	Gross Amounts Not Offset in the Consolidated Balance Sheet		
				Derivative Financial Instruments	Cash Collateral Received (Pledged)	Net Amount
Derivative assets	\$ 21,819	\$ —	\$ 21,819	\$ (4,091)	\$ —	\$ 17,728
Derivative liabilities	(4,091)	—	(4,091)	4,091	—	—

7. Inventories

Inventories consisted of the following (in thousands):

	December 31,	
	2024	2023
Raw materials	\$ 20,161	\$ 25,595
Work in process	311,752	431,732
Finished goods	148,532	139,712
Total inventories	<u>\$ 480,445</u>	<u>\$ 597,039</u>

As of December 31, 2024 and 2023, inventories included \$191.2 million and \$328.0 million, respectively, related to the purchase accounting inventory fair value step-up on inventory acquired as part of our GW Acquisition.

8. Property, Plant and Equipment

Property, plant and equipment consisted of the following (in thousands):

	December 31,	
	2024	2023
Manufacturing equipment and machinery	\$ 87,451	\$ 82,897
Land and buildings	71,902	70,912
Leasehold improvements	70,201	67,722
Computer software	42,635	38,134
Construction-in-progress	34,493	18,661
Computer equipment	20,137	15,398
Furniture and fixtures	8,551	9,273
Subtotal	335,370	302,997
Less accumulated depreciation and amortization	(161,957)	(133,351)
Property, plant and equipment, net	<u>\$ 173,413</u>	<u>\$ 169,646</u>

Depreciation and amortization expense on property, plant and equipment amounted to \$32.8 million, \$30.4 million and \$30.3 million for the years ended December 31, 2024, 2023 and 2022, respectively.

9. Goodwill and Intangible Assets

The gross carrying amount of goodwill was as follows (in thousands):

Balance at December 31, 2023	\$ 1,753,130
Foreign exchange	(36,807)
Balance at December 31, 2024	<u>\$ 1,716,323</u>

The gross carrying amounts and net book values of our intangible assets were as follows (in thousands):

	December 31, 2024				December 31, 2023			
	Remaining Weighted-Average Useful Life (In years)	Gross Carrying Amount	Accumulated Amortization	Net Book Value	Gross Carrying Amount	Accumulated Amortization	Net Book Value	
Acquired developed technologies	7.8	\$ 7,699,423	\$ (2,943,728)	\$ 4,755,695	\$ 7,785,495	\$ (2,367,456)	\$ 5,418,039	
Manufacturing contracts	—	11,121	(11,121)	—	11,828	(11,828)	—	
Trademarks	—	2,868	(2,868)	—	2,886	(2,886)	—	
Total finite-lived intangible assets		\$ 7,713,412	\$ (2,957,717)	\$ 4,755,695	\$ 7,800,209	\$ (2,382,170)	\$ 5,418,039	

The decrease in the gross carrying amount of intangible assets as of December 31, 2024 compared to December 31, 2023 primarily relates to the negative impact of foreign currency translation adjustments due to the weakening of sterling and euro against the U.S. dollar.

The assumptions and estimates used to determine future cash flows and remaining useful lives of our intangible and other long-lived assets are complex and subjective. They can be affected by various factors, including external factors, such as industry and economic trends, and internal factors such as changes in our business strategy and our forecasts for specific product lines.

Based on finite-lived intangible assets recorded as of December 31, 2024, and assuming the underlying assets will not be impaired and that we will not change the expected lives of any other assets, future amortization expenses were estimated as follows (in thousands):

<u>Year Ending December 31,</u>	<u>Estimated Amortization Expense</u>
2025	\$ 618,043
2026	618,043
2027	618,043
2028	616,711
2029	614,977
Thereafter	1,669,878
Total	<u>\$ 4,755,695</u>

10. Accrued Liabilities

Accrued liabilities consisted of the following (in thousands):

	December 31,	
	2024	2023
Rebates and other sales deductions	\$ 342,717	\$ 325,711
Employee compensation and benefits	153,133	121,209
Clinical trial accruals	49,962	44,757
Accrued interest	41,626	36,443
Accrued royalties	36,802	30,706
Accrued milestones	27,500	—
Selling and marketing accruals	26,981	14,743
Sales return reserve	26,428	20,435
Consulting and professional services	26,221	19,538
Inventory-related accruals	25,509	13,977
Accrued development expenses	23,099	15,431
Accrued collaboration expenses	18,005	10,158
Current portion of lease liabilities	14,779	19,447
Derivative instrument liabilities	10,198	681
Accrued construction-in-progress	10,061	5,141
Accrued facilities expenses	6,107	55,455
Other	71,819	60,082
Total accrued liabilities	<u>\$ 910,947</u>	<u>\$ 793,914</u>

11. Debt

The following table summarizes the carrying amount of our indebtedness (in thousands):

	December 31,	
	2024	2023
2024 Notes	\$ —	\$ 575,000
Unamortized - debt issuance costs	—	(1,046)
2024 Notes, net	—	573,954
2026 Notes	1,000,000	1,000,000
Unamortized - debt issuance costs	(3,747)	(6,400)
2026 Notes, net	996,253	993,600
2030 Notes	1,000,000	—
Unamortized - debt issuance costs	(19,135)	—
2030 Notes, net	980,865	—
Secured Notes	1,483,841	1,480,214
Term Loan	2,647,681	2,665,174
Total debt	6,108,640	5,712,942
Less current portion ⁽¹⁾	31,000	604,954
Total long-term debt	<u>\$ 6,077,640</u>	<u>\$ 5,107,988</u>

(1) Balance as of December 31, 2023 includes the 2024 Notes as they matured in August 2024.

Credit Agreement

On May 5, 2021, Jazz Pharmaceuticals plc, Jazz Lux, and certain of our other subsidiaries, as borrowers, or, collectively with Jazz Pharmaceuticals plc and Jazz Lux, the “Borrowers”, entered into the Credit Agreement. The Credit Agreement initially provided for (i) the Dollar Term Loan, which was drawn by Jazz Lux on the closing date thereof in U.S. dollars (ii) the Euro Term Loan, which was drawn by Jazz Lux on the closing date thereof in Euros and (iii) the Initial Revolving Credit Facility.

We used the proceeds from the Dollar Term Loan (i) to repay in full \$575.9 million under the 2015 Credit Agreement, (ii) to fund, in part, the cash consideration payable in connection with the GW Acquisition and (iii) to pay related fees and expenses. Upon the repayment in full of loans under the 2015 Credit Agreement, it was terminated and all guarantees and liens thereunder were released.

In 2021, we made voluntary prepayments on the Euro Term Loan totaling €416.7 million, or \$502.0 million, and in March 2022 we repaid the remaining outstanding principal of €208.3 million, or \$251.0 million. The Euro Term Loan bore interest at the EURIBOR plus an applicable margin. During the term of the Euro Term Loan, the interest rate and effective interest rate were 4.43% and 4.93%, respectively.

In January 2024, Jazz Lux entered into the Repricing Amendment No.1 to the Credit Agreement. Upon entry into the Repricing Amendment No.1, certain existing lenders converted a portion of the outstanding Dollar Term Loan into the Tranche B-1 Dollar Term Loans, and Jazz Lux borrowed \$201.9 million aggregate principal amount of additional Tranche B-1 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Dollar Term Loan that was not converted.

In July 2024, Jazz Lux entered into the Repricing Amendment No. 2 to the Credit Agreement, as amended by the Repricing Amendment No. 1. Upon entry into Repricing Amendment No. 2, certain existing lenders converted a portion of the outstanding Tranche B-1 Dollar Term Loans into the Tranche B-2 Dollar Term Loans, and Jazz Lux borrowed \$289.6 million aggregate principal amount of additional Tranche B-2 Dollar Term Loans, the proceeds of which were used to repay the portion of the outstanding Tranche B-1 Dollar Term Loans that were not converted.

The Tranche B-2 Dollar Term Loans are a separate class of term loans under the Credit Agreement, as amended by Repricing Amendment No. 1 and Repricing Amendment No. 2, with the same material terms (including with respect to maturity, prepayment, security, covenants and events of default) as the previously outstanding Tranche B-1 Dollar Term Loans and the initial Dollar Term Loan incurred on May 5, 2021, with the interest rate amended as described below and the credit spread adjustment removed. The principal amount of Tranche B-1 Dollar Term Loans outstanding immediately prior to the Repricing Amendment No. 2 and the outstanding principal amount of Tranche B-2 Dollar Term Loans immediately following the Repricing Amendment No.2, each totaled \$2.7 billion.

The Tranche B-2 Dollar Term Loans bear interest at a rate equal to either (a) Term SOFR or (b) the prime lending rate, in each case, plus an applicable margin. The applicable margin for the Tranche B-2 Dollar Term Loans is 2.25% (in the case of Term SOFR borrowings) and 1.25% (in the case of borrowings at the prime lending rate), a decrease, in each case, of 75 basis points from the applicable margin on the Tranche B-1 Dollar Term Loans. The Tranche B-2 Dollar Term Loans are subject to a Term SOFR floor of 0.50%. As of December 31, 2024, the interest rate and effective interest rate on the Tranche B-2 Dollar Term Loans were 6.61% and 8.27%, respectively.

In November 2024, we entered into Amendment No. 3 to the Credit Agreement, as amended by the Repricing Amendment No. 1 and Repricing Amendment No. 2, to increase the Initial Revolving Credit Facility from \$500.0 million to \$885.0 million and extend the maturity date, or Amended Revolving Credit Facility, from May 5, 2026 to November 26, 2029 (such date, the “Amended Revolving Facility Maturity Date”), provided that:

- if, as of any date from March 16, 2026 to the maturity date of the 2026 Notes (any such date, the “2026 Notes Springing Maturity Date”), (x) any 2026 Notes (or any permitted refinancing indebtedness in respect thereof with a maturity date that is not later than the date that is 91 days after the Amended Revolving Facility Maturity Date) (any such indebtedness, the “2026 Maturity Indebtedness”) remain outstanding and (y) the aggregate amount of unrestricted cash of Jazz Pharmaceuticals plc and its subsidiaries is less than an amount equal to 125% of the aggregate principal amount of 2026 Maturity Indebtedness outstanding, then the maturity date for the Amended Revolving Credit Facility will be shortened to the 2026 Notes Springing Maturity Date;
- if, as of February 4, 2028, (x) more than \$500,000,000 of the Tranche B-2 Dollar Term Loans under the Amended Credit Agreement (and any extended term loans, refinancing term loans, refinancing notes and permitted refinancing indebtedness, in each case, in respect thereof) (any such indebtedness, the “Term Loan Indebtedness”) remains outstanding and (y) the maturity date of such Term Loan Indebtedness is not later than the date that is 91 days after

the Amended Revolving Facility Maturity Date, then the maturity date for the Amended Revolving Credit Facility will be shortened to February 4, 2028; and

- if, as of October 16, 2028 (such date, the “Senior Notes Springing Maturity Date”), (x) more than \$500,000,000 of the Secured Notes (and permitted refinancing indebtedness in respect thereof) (any such indebtedness, the “Senior Note Indebtedness”) remains outstanding and (y) the maturity date with respect to such Senior Note Indebtedness is not later than the date that is 91 days after the Amended Revolving Facility Maturity Date, then the maturity date for the Amended Revolving Credit Facility will be shortened to October 16, 2028.

Initially, the applicable margin for the loans under the Amended Revolving Credit Facility will be 2.00% (in the case of Term SOFR borrowings) and 1.00% (in the case of borrowings at the prime lending rate). Thereafter, the applicable margin for the Amended Revolving Credit Facility ranges from 1.75% to 2.75% (in the case of Term SOFR borrowings) and 0.75% to 1.75% (in the case of borrowings at the prime lending rate), depending on our first lien secured net leverage ratio level, and any loans under the Amended Revolving Credit Facility are subject to a Term SOFR floor of 0.00%. The Amended Revolving Credit Facility has a commitment fee payable on the undrawn amount ranging from 0.25% to 0.45% per annum based upon our first lien secured net leverage ratio. As of December 31, 2024, we had an undrawn Amended Revolving Credit Facility totaling \$885.0 million.

We may make voluntary prepayments at any time without payment of a premium or penalty, subject to certain exceptions, and are required to make certain mandatory prepayments of outstanding indebtedness under the Amended Credit Agreement in certain circumstances. Principal repayments of the Dollar Term Loan, which were due quarterly, began in September 2021 and were equal to 1.0% per annum of the original principal amount of \$3.1 billion with any remaining balance payable on the maturity date. In September 2022, we made a voluntary repayment on the Dollar Term Loan totaling \$300.0 million. In January 2025, we made a voluntary repayment on the Tranche B-2 Dollar Term Loans totaling \$750.0 million. The Tranche B-2 Dollar Term Loans will amortize in quarterly installments equal to 0.286294791% of the initial aggregate principal amount thereof, with the remaining balance payable on May 5, 2028.

Our obligations under the Amended Credit Agreement and any hedging or cash management obligations entered into with any lender thereunder are guaranteed by Jazz Pharmaceuticals plc, the other borrowers, and each of the Jazz Pharmaceuticals plc’s other existing or subsequently acquired or organized direct and indirect subsidiaries (subject to certain exceptions), or the Guarantors. We refer to the Borrowers and the Guarantors collectively as the “Loan Parties.”

The Loan Parties’ obligations under the Amended Credit Agreement are secured, subject to customary permitted liens and other exceptions, by a security interest in (a) all tangible and intangible assets of the Loan Parties, except for certain excluded assets, and (b) all of the equity interests of the subsidiaries of the Loan Parties held by the Loan Parties.

The Amended Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants applicable to Jazz Pharmaceuticals plc and its restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. The Amended Credit Agreement contains financial covenants that require Jazz Pharmaceuticals plc and its restricted subsidiaries to (a) not exceed a maximum first lien secured net leverage ratio and (b) not fall below a minimum interest coverage ratio, provided that such covenants apply only to the Amended Revolving Credit Facility and are applicable only if amounts are drawn (or non-cash collateralized letters of credit in excess of \$50.0 million are outstanding) under the Amended Revolving Credit Facility. The Amended Credit Agreement also contains customary events of default relating to, among other things, failure to make payments, breach of covenants and breach of representations.

2029 Senior Secured Notes

On April 29, 2021, Jazz Securities, a wholly owned subsidiary of Jazz Pharmaceuticals plc, closed the offering of the Secured Notes in a private placement. We used the proceeds from the Secured Notes to fund, in part, the cash consideration payable in connection with the GW Acquisition.

Interest on the Secured Notes is payable semi-annually in arrears on January 15 and July 15 of each year, beginning on January 15, 2022, at a rate of 4.375% per year. The Secured Notes mature on January 15, 2029.

The Secured Notes are jointly and severally guaranteed by Jazz Pharmaceuticals plc and each of its restricted subsidiaries, other than Jazz Securities, that is a borrower, or a guarantor, under the Amended Credit Agreement. The Secured Notes and related guarantees are secured by a first priority lien (subject to permitted liens and certain other exceptions), equally and ratably with the Amended Credit Agreement, on the collateral securing the Amended Credit Agreement.

Some or all of the Secured Notes, may be redeemed at any time and from time to time at a specified redemption prices, plus accrued and unpaid interest, if any, to, but excluding, to the redemption date. In addition, Jazz Securities may redeem all

but not part of the Secured Notes at its option at any time in connection with certain tax-related events at a price equal to 100% of the principal amount of the Secured Notes to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date.

If Jazz undergoes a change of control, Jazz Securities will be required to make an offer to purchase all of the Secured Notes at a purchase price in cash equal to 101% of the principal amount thereof, plus accrued and unpaid interest, if any, to, but excluding, the date of repurchase, subject to certain exceptions.

The indenture governing the Secured Notes contains customary affirmative covenants and negative covenants applicable to Jazz Pharmaceuticals plc and its restricted subsidiaries, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of junior indebtedness and dividends and other distributions. If Jazz Securities or Jazz Pharmaceuticals plc's restricted subsidiaries engage in certain asset sales, Jazz Securities will be required under certain circumstances to make an offer to purchase the Secured Notes at 100% of the principal amount, plus accrued and unpaid interest, if any, to, but excluding, the repurchase date.

As of December 31, 2024, the interest rate and effective interest rate on the Secured Notes were 4.375% and 4.64%, respectively.

2030 Notes

In September 2024, Jazz Investments, a wholly owned subsidiary of Jazz Pharmaceuticals plc, completed a private placement of \$1.0 billion principal amount of the 2030 Notes.

Interest on the 2030 Notes is payable semi-annually in cash in arrears on March 15 and September 15 of each year, beginning on March 15, 2025, at a rate of 3.125% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2030 Notes. The 2030 Notes mature on September 15, 2030, unless earlier exchanged, redeemed or repurchased.

The holders of the 2030 Notes have the ability to require us to repurchase all or a portion of their 2030 Notes for cash at a fundamental change repurchase price equal to 100% of the principal amount of the notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date in the event we undergo a fundamental change (as defined in the indenture related to the 2030 Notes), such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from any of The New York Stock Exchange, The Nasdaq Global Market, The Nasdaq Global Select Market or The Nasdaq Capital Market (or any of their respective successors).

Additionally, the terms and covenants in the indenture related to the 2030 Notes include certain events of default after which the 2030 Notes may be due and payable immediately.

Prior to September 15, 2030, we may redeem the 2030 Notes, in whole but not in part, in connection with certain tax-related events. We also may redeem the 2030 Notes on or after September 20, 2027 and prior to June 15, 2030, in whole or in part (subject to the partial redemption limitation described in the indenture related to the 2030 Notes), if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide notice of redemption at a redemption price equal to 100% of the principal amount of the notes to be redeemed, plus accrued and unpaid interest to, but excluding, the redemption date.

The 2030 Notes are exchangeable at an initial exchange rate of 6.5339 ordinary shares per \$1,000 principal amount of 2030 Notes, which is equivalent to an initial exchange price of approximately \$153.05 per ordinary share. Upon exchange of the 2030 Notes, we will pay cash up to the aggregate principal amount of the 2030 Notes to be exchanged and pay or deliver, as the case may be, cash, ordinary shares or a combination of cash and ordinary shares, at our election, in respect of the remainder, if any, of our exchange obligation in excess of the aggregate principal amount of the 2030 Notes being exchanged. The exchange rate is subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes (as defined in the indenture related to the 2030 Notes) that occur prior to the maturity date or upon our issuance of a notice of redemption, we will, in certain circumstances, increase the exchange rate for a holder who elects to exchange its 2030 Notes in connection with that make-whole fundamental change or exchange its 2030 Notes called (or deemed called) for redemption during the related redemption period. Prior to June 15, 2030, the 2030 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

As of December 31, 2024, the "if converted value" did not exceed the principal amount of the 2030 Notes.

The total liability is reflected net of issuance costs of \$19.2 million which will be amortized over the term of the 2030 Notes. We have determined the expected life of the 2030 Notes to be equal to the original six-year term. The effective interest rate of the 2030 Notes is 3.47%.

2026 Notes

In 2020 we completed a private placement of \$1.0 billion principal amount of the 2026 Notes. We used a portion of the net proceeds from this offering to repurchase for cash \$332.9 million aggregate principal amount of the 1.875% exchangeable senior notes due 2021, through privately-negotiated transactions concurrently with the offering of the 2026 Notes. Interest on the 2026 Notes is payable semi-annually in cash in arrears on June 15 and December 15 of each year, beginning on December 15, 2020, at a rate of 2.00% per year. In certain circumstances, we may be required to pay additional amounts as a result of any applicable tax withholding or deductions required in respect of payments on the 2026 Notes. The 2026 Notes mature on June 15, 2026, unless earlier exchanged, repurchased or redeemed.

The holders of the 2026 Notes have the ability to require us to repurchase all or a portion of their 2026 Notes for cash in the event we undergo certain fundamental changes, such as specified change of control transactions, our liquidation or dissolution or the delisting of our ordinary shares from any of The New York Stock Exchange, The Nasdaq Global Market, The Nasdaq Global Select Market or The Nasdaq Capital Market (or any of their respective successors). Additionally, the terms and covenants in the indenture related to the 2026 Notes include certain events of default after which the 2026 Notes may be due and payable immediately. Prior to June 15, 2026, we may redeem the 2026 Notes, in whole but not in part, subject to compliance with certain conditions, if we have, or on the next interest payment date would, become obligated to pay to the holder of any 2026 Notes additional amounts as a result of certain tax-related events. We also may redeem the 2026 Notes prior to March 15, 2026, in whole or in part, if the last reported sale price per ordinary share has been at least 130% of the exchange price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading day period ending on, and including, the trading day immediately preceding the date on which we provide the notice of redemption.

The 2026 Notes are exchangeable at an initial exchange rate of 6.4182 ordinary shares per \$1,000 principal amount of 2026 Notes, which is equivalent to an initial exchange price of approximately \$155.81 per ordinary share. On July 22, 2024, we irrevocably elected to fix the settlement method for exchanges of the 2026 Notes to a combination of cash and ordinary shares of Jazz Pharmaceuticals plc with a specified cash amount per \$1,000 principal amount of 2026 Notes exchanged equal to or in excess of \$1,000. As a result, for any 2026 Notes exchanged subsequent to such notice, an exchanging holder will receive (i) up to \$1,000 in cash per \$1,000 principal amount of 2026 Notes exchanged and (ii) cash, ordinary shares, or any combination thereof, at our election, in respect of the remainder, if any, of its exchange obligation in excess of \$1,000 per \$1,000 principal amount of 2026 Notes exchanged. The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain make-whole fundamental changes occurring prior to the maturity date of the 2026 Notes or upon our issuance of a notice of redemption, we will in certain circumstances increase the exchange rate for holders of the 2026 Notes who elect to exchange their 2026 Notes in connection with that make-whole fundamental change or during the related redemption period. Prior to March 15, 2026, the 2026 Notes will be exchangeable only upon satisfaction of certain conditions and during certain periods, and thereafter, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date.

As of December 31, 2024 and 2023, the “if converted value” did not exceed the principal amount of the 2026 Notes.

The total liability is reflected net of issuance costs of \$15.3 million which will be amortized over the term of the 2026 Notes. We have determined the expected life of the 2026 Notes to be equal to the original six-year term. The effective interest rate of the 2026 Notes is 2.26%.

2024 Notes

In 2017, we completed a private placement of \$575.0 million principal amount of 2024 Notes. We used the net proceeds from this offering to repay \$500.0 million in outstanding loans under the Initial Revolving Credit Facility and to pay related fees and expenses. We used the remainder of the net proceeds for general corporate purposes. Interest on the 2024 Notes was payable semi-annually in cash in arrears on February 15 and August 15 of each year, beginning on February 15, 2018, at a rate of 1.50% per year. The 2024 Notes were exchangeable at an initial exchange rate of 4.5659 ordinary shares per \$1,000 principal amount of 2024 Notes, which was equivalent to an initial exchange price of approximately \$219.02 per ordinary share.

On August 15, 2024, the maturity date for the 2024 Notes, we repaid the \$575.0 million aggregate principal amount, plus accrued and unpaid interest thereon.

The Exchangeable Senior Notes were issued by Jazz Investments I Limited, or the Issuer, a 100%-owned finance subsidiary of Jazz Pharmaceuticals plc. The Exchangeable Senior Notes are senior unsecured obligations of the Issuer and are fully and unconditionally guaranteed on a senior unsecured basis by Jazz Pharmaceuticals plc. No subsidiary of Jazz Pharmaceuticals plc guaranteed the Exchangeable Senior Notes. Subject to certain local law restrictions on payment of dividends, among other things, and potential negative tax consequences, we are not aware of any significant restrictions on the ability of Jazz Pharmaceuticals plc to obtain funds from the Issuer or Jazz Pharmaceuticals plc's other subsidiaries by dividend or loan, or any legal or economic restrictions on the ability of the Issuer or Jazz Pharmaceuticals plc's other subsidiaries to transfer funds to Jazz Pharmaceuticals plc in the form of cash dividends, loans or advances. There is no assurance that in the future such restrictions will not be adopted.

For the year ended December 31, 2024, we recognized \$40.0 million, in interest expense, net, of which \$35.3 million related to the contractual coupon rate and \$4.7 million related the amortization of the debt issuance costs on the 2024 Notes and the Exchangeable Senior Notes. For the years ended December 31, 2023 and 2022, we recognized \$32.8 million in interest expense, net, of which \$28.6 million related to the contractual coupon rate and \$4.2 million related to the amortization of the debt issuance costs.

Scheduled maturities with respect to our long-term debt are as follows (in thousands):

<u>Year Ending December 31,</u>	<u>Scheduled Long-Term Debt Maturities</u>
2025	\$ 31,000
2026	1,031,000
2027	31,000
2028	2,598,500
2029	1,500,000
Thereafter	1,000,000
Total	\$ 6,191,500

12. Leases

We have noncancelable leases for our buildings and growing facilities and we are obligated to make payments under noncancelable operating leases for automobiles used by our sales force.

The components of the lease expense for the years ended December 31, 2024, 2023 and 2022 were as follows (in thousands):

<u>Lease Cost</u>	<u>Year Ended December 31,</u>		
	<u>2024</u>	<u>2023</u>	<u>2022</u>
Operating lease cost	\$ 22,209	\$ 19,394	\$ 19,670
Short-term lease cost	7,441	6,290	5,088
Variable lease cost	789	81	5
Sublease income	(472)	(22)	—
Finance Lease Cost			
Interest on lease liabilities	442	377	429
Amortization of leased asset	413	481	472
Net lease cost	\$ 30,822	\$ 26,601	\$ 25,664

Supplemental balance sheet information related to operating and finance leases was as follows (in thousands):

Leases	Classification	December 31,	
		2024	2023
Assets			
Operating lease assets	Operating lease assets	\$ 53,582	\$ 65,340
Finance lease assets	Property, plant and equipment	3,917	4,450
Total lease assets		<u>\$ 57,499</u>	<u>\$ 69,790</u>
Liabilities			
Current			
Operating lease liabilities	Accrued liabilities	\$ 14,331	\$ 19,019
Finance lease liabilities	Accrued liabilities	448	428
Non-current			
Operating lease liabilities	Operating lease liabilities, less current portion	38,938	59,225
Finance lease liabilities	Other non-current liabilities	4,561	5,039
Total lease liabilities		<u>\$ 58,278</u>	<u>\$ 83,711</u>
		December 31,	
Lease Term and Discount Rate		2024	2023
Weighted-average remaining lease term (years)			
Operating leases		4.3	5.1
Finance leases		10.4	11.2
Weighted-average discount rate			
Operating leases		6.6 %	5.4 %
Finance leases		7.6 %	7.5 %

Supplemental cash flow information related to operating and finance leases was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Cash paid for amounts included in the measurement of lease liabilities:			
Operating cash outflows from operating leases	\$ 33,632	\$ 20,646	\$ 20,544
Operating cash outflows from finance leases	830	835	806
Financing cash outflows from finance leases	442	377	429
Non-cash operating activities:			
Operating lease assets obtained in exchange for new operating lease liabilities	\$ 25,819	\$ 9,953	\$ 4,312
De-recognition of operating lease asset on lease assignment / termination	19,877	4,169	—
De-recognition of operating lease liability on lease assignment / termination	21,297	4,457	—

Maturities of operating and finance lease liabilities were as follows (in thousands):

<u>Year Ending December 31,</u>	<u>Operating Leases</u>	<u>Finance Leases</u>
2025	\$ 16,574	\$ 837
2026	12,596	811
2027	10,314	758
2028	9,020	601
2029	6,036	601
Thereafter	8,344	3,717
Total lease payments	62,884	7,325
Less imputed interest	(9,615)	(2,316)
Present value of lease liabilities	\$ 53,269	\$ 5,009

On October 11, 2024, we entered into a new lease agreement for premises located at 3000 El Camino Real, Palo Alto, California, with occupancy expected by July 1, 2025. The lease will be recognized on the lease commencement date with the lease ending in 2035.

13. Commitments and Contingencies

Indemnification

In the normal course of business, we enter into agreements that contain a variety of representations and warranties and provide for general indemnification, including indemnification associated with product liability or infringement of intellectual property rights. Our exposure under these agreements is unknown because it involves future claims that may be made but have not yet been made against us. To date, we have not paid any claims or been required to defend any action related to these indemnification obligations.

We have agreed to indemnify our executive officers, directors and certain other employees for losses and costs incurred in connection with certain events or occurrences, including advancing money to cover certain costs, subject to certain limitations. The maximum potential amount of future payments we could be required to make under the indemnification obligations is unlimited; however, we maintain insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe the fair value of these indemnification obligations is not significant. Accordingly, we did not recognize any liabilities relating to these obligations as of December 31, 2024 and December 31, 2023. No assurances can be given that the covering insurers will not attempt to dispute the validity, applicability, or amount of coverage without expensive litigation against these insurers, in which case we may incur substantial liabilities as a result of these indemnification obligations.

Other Commitments

As of December 31, 2024, we had \$46.3 million of noncancelable purchase commitments due within one year, primarily related to agreements with third party manufacturers.

Legal Proceedings

We are involved in legal proceedings, including the following matters:

Xyrem Antitrust Litigation

From June 2020 to May 2022, a number of lawsuits were filed on behalf of purported direct and indirect Xyrem purchasers, alleging that the patent litigation settlement agreements we entered with generic drug manufacturers who had filed ANDAs violate state and federal antitrust and consumer protection laws, as follows:

On June 17, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by BCBS against the Company Defendants. The BCBS Lawsuit also the BCBS Defendants.

On June 18 and June 23, 2020, respectively, two additional class action lawsuits were filed against the Company Defendants and the BCBS Defendants: one by the New York State Teamsters Council Health and Hospital Fund in the United States District Court for the Northern District of California, and another by the Government Employees Health Association Inc. in the United States District Court for the Northern District of Illinois.

On June 18, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of California by the City of Providence, Rhode Island, on behalf of itself and all others similarly situated, against the City of Providence Defendants.

On June 30, 2020, a class action lawsuit was filed in the United States District Court for the Northern District of Illinois by UFCW Local 1500 Welfare Fund on behalf of itself and all others similarly situated, against UFCW Defendants.

On July 13, 2020, the plaintiffs in the BCBS Lawsuit and the GEHA Lawsuit dismissed their complaints in the United States District Court for the Northern District of Illinois and refiled their respective lawsuits in the United States District Court for the Northern District of California. On July 14, 2020, the plaintiffs in the UFCW Lawsuit dismissed their complaint in the United States District Court for the Northern District of Illinois and on July 15, 2020, refiled their lawsuit in the United States District Court for the Northern District of California.

On July 31, 2020, a class action lawsuit was filed in the United States District Court for the Southern District of New York by the A.F. of L.-A.G.C. Building Trades Welfare Plan on behalf of itself and all others similarly situated, against Jazz Pharmaceuticals plc. The AFL Plan Lawsuit also names Roxane Laboratories Inc., West-Ward Pharmaceuticals Corp., Hikma Labs Inc., Hikma Pharmaceuticals plc, Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc.

On August 14, 2020, an additional class action lawsuit was filed in the United States District Court for the Southern District of New York by the Self-Insured Schools of California on behalf of itself and all others similarly situated, against the Company Defendants, as well as Hikma Pharmaceuticals plc, Eurohealth (USA) Inc., Hikma Pharmaceuticals USA, Inc., West-Ward Pharmaceuticals Corp., Roxane Laboratories, Inc., Amneal Pharmaceuticals LLC, Endo International, plc, Endo Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals Inc., Lupin Inc., Sun Pharmaceutical Industries Ltd., Sun Pharmaceutical Holdings USA, Inc., Sun Pharmaceutical Industries, Inc., Ranbaxy Laboratories Ltd., Teva Pharmaceutical Industries Ltd., Watson Laboratories, Inc., Wockhardt Ltd., Morton Grove Pharmaceuticals, Inc., Wockhardt USA LLC, Mallinckrodt plc, and Mallinckrodt LLC.

On September 16, 2020, an additional class action lawsuit was filed in the United States District Court for the Northern District of California, by Ruth Hollman on behalf of herself and all others similarly situated, against the same defendants named in the Self-Insured Schools Lawsuit.

In December 2020, the above cases were centralized and transferred to the United States District Court for the Northern District of California, where the multidistrict litigation will proceed for the purpose of discovery and pre-trial proceedings.

On March 18, 2021, United Healthcare Services, Inc. filed a lawsuit in the United States District Court for the District of Minnesota against the Company Defendants, Hikma Pharmaceuticals plc, Roxane Laboratories, Inc., Hikma Pharmaceuticals USA Inc., Eurohealth (USA) Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., and Lupin Pharmaceuticals, Inc., raising similar allegations. On March 24, 2021, the U.S. Judicial Panel on Multidistrict Litigation conditionally transferred the UHS Lawsuit to the United States District Court for the Northern District of California, where it was consolidated for discovery and pre-trial proceedings with the other cases.

On August 13, 2021, the United States District Court for the Northern District of California granted in part and denied in part the Company Defendants' motion to dismiss the complaints in the cases referenced above.

On October 8, 2021, Humana Inc. filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On October 8, 2021, Molina Healthcare Inc. filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On February 17, 2022, Health Care Service Corporation filed a lawsuit in the United States District Court for the Northern District of California against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations.

On April 19, 2023, the Court held a hearing on class certification in the consolidated multi-district litigation referenced above. On May 12, 2023, the Court granted the plaintiffs' motion and preliminarily certified classes of Xyrem purchasers seeking monetary and injunctive relief. The Court excluded Xywav purchasers from the classes. On April 26, 2024, we,

Hikma, and the plaintiffs filed motions for summary judgment. The Court held oral argument on these motions on July 19, 2024. On August 26, 2024, the Court issued a decision granting in part and denying in part the parties' motions for summary judgment. Certain administrative service organization plaintiffs filed a motion for reconsideration of a portion of the Court's summary judgment ruling. On December 16, 2024, the Court denied the motion for reconsideration. On January 15, 2025, Aetna, Inc., which is not a party to the consolidated multi-district litigation, filed a notice of appeal of the order denying reconsideration.

On June 13, 2024, we filed a motion to decertify the class. On June 28, 2024, the plaintiffs filed a motion to amend the definition of the certified class. The Court held oral argument on these motions on August 22, 2024. On October 18, 2024, the Court issued a decision denying our motion to decertify the class and granting the plaintiffs' motion to amend the class definition. On November 1, 2024, we filed a petition with the United States Court of Appeals for the Ninth Circuit seeking leave to appeal the Court's decision amending the class definition. On January 29, 2025, the Ninth Circuit denied our petition for permission to appeal. Trial in this matter has been rescheduled for May 19, 2025.

On January 13, 2023, Amneal Pharmaceuticals LLC, Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, notified the Court that they had reached a settlement-in-principle with the class action plaintiffs. On April 19, 2023, the Court held a hearing on a motion for preliminary approval of this proposed settlement. On May 12, 2023, the Court granted the motion for preliminary approval of the proposed settlement. On January 11, 2024, the Court held a hearing on the motion for final approval of the proposed settlement. The Court deferred ruling and scheduled a further hearing for final approval of the proposed settlement on April 17, 2024. During February and March 2024, the parties notified the Court of settlements between certain non-class action plaintiffs and each of Amneal and Lupin, and the Court dismissed those plaintiffs' claims against the applicable parties. On April 17, 2024, the Court issued an order granting the motion for final approval of the settlement between the class action plaintiffs, Amneal, and Lupin.

On December 11, 2023, Blue Cross and Blue Shield of Florida, Inc. and Health Options, Inc. filed a lawsuit in the United States District Court for the Middle District of Florida against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., and Eurohealth (USA), Inc., raising similar allegations. On January 23, 2024, the Blue Cross Florida case was transferred to the United States District Court for the Northern District of California and consolidated with the above referenced multidistrict litigation for pretrial purposes.

On May 9, 2022, Aetna, filed a lawsuit in the Superior Court of California for the County of Alameda against the Company Defendants, Hikma Pharmaceuticals plc, Hikma Pharmaceuticals USA Inc., Hikma Labs, Inc., Eurohealth (USA), Inc., Amneal Pharmaceuticals LLC, Par Pharmaceutical, Inc., Lupin Ltd., Lupin Pharmaceuticals, Inc., and Lupin Inc, raising similar allegations. On December 27, 2022, the Court granted in part and denied in part our motion to dismiss Aetna's complaint. As a result of that ruling, the generic defendants have been dismissed from the case, and certain of Aetna's claims against Jazz have been dismissed. On January 27, 2023, Aetna filed an amended complaint against Jazz. On March 22, 2023, we filed motions to dismiss and to strike portions of the amended complaint. On June 26, 2023, the Court granted our motions, and granted Aetna leave to further amend its complaint. On November 17, 2023, Aetna filed its second amended complaint. On February 2, 2024, we filed our answer to the second amended complaint and Hikma filed a motion to quash service. The Court scheduled a hearing on Hikma's motion for December 4, 2024. The Court has not set a further schedule in this case.

The plaintiffs in certain of these lawsuits are seeking to represent a class of direct purchasers of Xyrem, and the plaintiffs in the remaining lawsuits are seeking to represent a class of indirect purchasers of Xyrem. Each of the lawsuits generally alleges violations of U.S. federal and state antitrust, consumer protection, and unfair competition laws in connection with the Company Defendants' conduct related to Xyrem, including actions leading up to, and entering into, patent litigation settlement agreements with each of the other named defendants. Each of the lawsuits seeks monetary damages, exemplary damages, equitable relief against the alleged unlawful conduct, including disgorgement of profits and restitution, and injunctive relief. It is possible that additional lawsuits will be filed against the Company Defendants making similar or related allegations. If the plaintiffs were to be successful in their claims, they may be entitled to injunctive relief or we may be required to pay significant monetary damages, which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

Patent Infringement Litigation

Avadel Litigation

On May 13, 2021, we filed a patent infringement suit against Avadel, and several of its corporate affiliates in the United States District Court for the District of Delaware. The suit alleges that Avadel's Lumryz will infringe five of our patents related to controlled release formulations of oxybate and the safe and effective distribution of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe these patents, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid

or not enforceable, and that its product will not infringe our patents. Avadel filed a motion for partial judgment on the pleadings on its counterclaim that one of our patents should be delisted from the Orange Book. On November 18, 2022, the Court issued an order that we delist the patent from the Orange Book. On November 22, 2022, we filed a notice of appeal to the United States Court of Appeals for the Federal Circuit. The Federal Circuit temporarily stayed the District Court's delisting order. On February 24, 2023, the Federal Circuit affirmed the District Court's delisting order, lifted the temporary stay, and gave Jazz 14 days to request that FDA delist the patent from the Orange Book. Jazz complied with the Federal Circuit's order and requested delisting on February 28, 2023. On March 3, 2023, we and Avadel stipulated to the dismissal without prejudice of the claims and counterclaims related to infringement and validity of the delisted patent in both this suit and a later-filed suit described below related to the same patent.

On August 4, 2021, we filed an additional patent infringement suit against Avadel in the United States District Court for the District of Delaware. The second suit alleges that Avadel's Lumryz will infringe a newly-issued patent related to sustained-release formulations of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe this patent, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product will not infringe our patents.

On November 10, 2021, we filed an additional patent infringement suit against Avadel in the United States District Court for the District of Delaware. The third suit alleges that Avadel's Lumryz will infringe a newly-issued patent related to sustained-release formulations of oxybate. The suit seeks an injunction to prevent Avadel from launching a product that would infringe this patent, and an award of monetary damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product will not infringe our patents.

On April 14, 2022, Avadel sued us in the United States District Court for the District of Delaware. Avadel's suit alleges that we misappropriated trade secrets related to Avadel's once-nightly sodium oxybate development program and breached certain contracts between the parties. Avadel seeks monetary damages, an injunction preventing us from using Avadel's confidential information, and an order directing the United States Patent and Trademark Office to modify the inventorship of one of our oxybate patents. On July 8, 2022, we filed a motion for judgment on the pleadings, which the Court denied on July 18, 2023. The denial is not a ruling that Jazz misappropriated Avadel's trade secrets or breached any contract. The case will go forward in discovery and the Court instructed the parties to submit a proposed scheduling order.

On June 7, 2022, we received notice from Avadel that it had filed a "paragraph IV certification" regarding one patent listed in the Orange Book for Xyrem. A paragraph IV certification is a certification by a generic applicant that alleges that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product. On July 15, 2022, we filed an additional lawsuit against Avadel asserting infringement of that patent. The suit alleges that the filing of Avadel's application for approval of FT218 is an act of infringement, and that Avadel's product would infringe the patent if launched. The suit seeks an injunction to prevent Avadel from launching a product that would infringe the patent, and an award of damages if Avadel does launch an infringing product. Avadel filed an answer to the complaint and counterclaims asserting that the patent is invalid, that its product would not infringe, and that by listing the patent in the Orange Book, we engaged in unlawful monopolization in violation of the Sherman Act. On December 9, 2022, we filed a motion to dismiss Avadel's counterclaims. On June 29, 2023, we filed a motion seeking leave to supplement our motion to dismiss, as well as a motion to stay discovery pending resolution of the motion to dismiss. As noted above, on March 3, 2023, we and Avadel stipulated to the dismissal without prejudice of the claims and counterclaims related to infringement and validity of the delisted patent.

On November 1, 2023, the Court held a claim construction hearing relating to disputed terms in the asserted patents. On December 15, 2023, the Court issued a written opinion and order resolving the parties' remaining claim construction disputes. On November 20, 2023, we and Avadel each filed motions for summary judgment. On February 14, 2024, the Court issued a written opinion and order denying both parties' motions for summary judgment.

Trial regarding our patent infringement claims against Avadel began on February 26, 2024, and concluded on March 4, 2024, with the jury finding both of our asserted patents valid, and awarding us damages for infringement for Avadel's past sales of Lumryz. On April 12, 2024, we filed a motion for a permanent injunction and ongoing royalties. On August 27, 2024, the Court granted our motion for an injunction in part, and requested additional briefing about ongoing royalties. The issued injunction prevents Avadel from seeking FDA approval or marketing Lumryz for the treatment of idiopathic hypersomnia or other indications not already a part of Lumryz's product labeling as of March 4, 2024, and enjoins Avadel from infringing in any way Claim 24 of our '782 patent by making, using or selling Lumryz through and including the February 2036 expiration date of the '782 patent, subject to certain exclusions including, among other things (i) for the treatment of narcolepsy, (ii) for the treatment of patients who have been prescribed Lumryz as of the effective date of the

injunction conditioned on the payment of an amount to be determined and (iii) in clinical trials and studies ongoing as of the effective date of the injunction. The Court also granted our motion for an ongoing royalty for any future sale of Lumryz to patients with narcolepsy at a rate to be determined based upon further briefing by the parties on the appropriate ongoing rate above 3.5%. Avadel is appealing this injunction to the United States Court of Appeals for the Federal Circuit. The Federal Circuit held oral argument on this appeal on February 7, 2025, but has not yet issued a decision. Avadel filed a motion with the district court for a stay of the injunction pending appeal, which the district court denied. Avadel also filed a motion to stay the injunction pending appeal with the Federal Circuit, which the Federal Circuit granted to the limited extent that the injunction enjoins initiating new clinical trials or studies and denied in all other respects.

The Court scheduled a trial regarding Avadel's counterclaims for unlawful monopolization for November 3, 2025 and a trial regarding Avadel's trade secret misappropriation claims for December 15, 2025. On March 13, 2024 and March 19, 2024, we filed motions to stay Avadel's unlawful monopolization counterclaim and trade secret claims, respectively, pending resolution of post-trial motions and potential appeals in the patent infringement suit. On May 24, 2024, the Court denied the motion to stay the unlawful monopolization counterclaim and the previously-filed motion to dismiss the same. On June 7, 2024, we filed a motion for reargument or, in the alternative, to certify the decision for interlocutory appeal. That motion remains pending and no hearing date has been set. The Court stayed Avadel's trade secret misappropriation claims pending appeal of the injunction in the related patent matter. We filed a further motion to stay the unlawful monopolization counterclaims, which remains pending.

On July 21, 2022, Avadel filed a lawsuit against FDA in the United States District Court for the District of Columbia, challenging FDA's determination that Avadel was required to file a paragraph IV certification regarding one of our Orange Book listed patents. Avadel filed a motion for preliminary injunction or, in the alternative, summary judgment, seeking relief including a declaration that FDA's decision requiring patent certification was unlawful, an order setting aside that decision, an injunction prohibiting FDA from requiring such certification as a precondition to approval of its application for FT218, and an order requiring FDA to take final action on Avadel's application for approval of FT218 within 14 days of the Court's ruling. On July 27, 2022, we filed a motion to intervene in that case, which the Court granted. The Court held a hearing on the parties' respective motions for summary judgment on October 7, 2022. On November 3, 2022, the Court granted our and FDA's motions for summary judgment and denied Avadel's motion.

From December 2024 through February 2025, Avadel filed a series of patent infringement suits against us in the United States District Court for the District of Delaware. The suits allege that Jazz's sales of Xywav infringe on certain newly-issued Avadel patents, and Avadel seeks an award of monetary damages. We have not yet responded to these lawsuits.

Xywav Patent Litigation

In June 2021, we received notice from Lupin, that it has filed with FDA an ANDA, for a generic version of Xywav. The notice from Lupin included a paragraph IV certification with respect to ten of our patents listed in FDA's Orange Book for Xywav on the date of our receipt of the notice. The asserted patents relate generally to the composition and method of use of Xywav, and methods of treatment when Xywav is administered concomitantly with certain other medications.

In July 2021, we filed a patent infringement suit against Lupin in the United States District Court for the District of New Jersey. The complaint alleges that by filing its ANDA, Lupin has infringed ten of our Orange Book listed patents. We are seeking a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patents. As a result of this lawsuit, we expect that a stay of approval of up to 30 months will be imposed by FDA on Lupin's ANDA. In June 2021, FDA recognized seven years of Orphan Drug Exclusivity for Xywav through July 21, 2027. On October 4, 2021, Lupin filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

In April 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On May 11, 2022, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent related to a method of treatment when Xywav is administered concomitantly with certain other medications. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe our patent. On June 22, 2022, the Court consolidated the two lawsuits we filed against Lupin.

In November 2022, we received notice from Lupin that it had filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On January 19, 2023, we filed an additional lawsuit against Lupin in the United States District Court for the District of New Jersey alleging that by filing its ANDA, Lupin infringed the newly-issued patent referenced in its November 2022 paragraph IV certification, as well as another patent that issued in January 2023. The suit seeks a permanent injunction to prevent Lupin from introducing a generic version of Xywav that would infringe the two patents

in suit. On February 15, 2023, the Court consolidated the new lawsuit with the two suits we previously filed against Lupin. No trial date has been set in the consolidated case against Lupin.

In February 2023, we received notice from Teva that it had filed with FDA an ANDA for a generic version of Xywav. The notice from Teva included a paragraph IV certification with respect to thirteen of our patents listed in FDA's Orange Book for Xywav on the date of the receipt of the notice. The asserted patents relate generally to the composition and method of use of Xywav, and methods of treatment when Xywav is administered concomitantly with certain other medications.

In March 2023, we filed a patent infringement suit against Teva in the United States District Court for the District of New Jersey. The complaint alleges that by filing its ANDA, Teva has infringed thirteen of our Orange Book listed patents. We are seeking a permanent injunction to prevent Teva from introducing a generic version of Xywav that would infringe our patents. As a result of this lawsuit, we expect that a stay of approval of up to 30 months will be imposed by FDA on Teva's ANDA. On May 23, 2023, Teva filed an answer to the complaint and counterclaims asserting that the patents are invalid or not enforceable, and that its product, if approved, will not infringe our patents.

On December 15, 2023, based on a stipulation between all parties, the Court consolidated the Lupin lawsuits and the Teva lawsuit for all purposes. No trial date has been set in the consolidated case.

In July 2024, we received notices from Lupin and Teva that they had each filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Xywav. On August 27, 2024, we filed an additional lawsuit in the United States District Court for the District of New Jersey against each of Lupin and Teva, alleging that, by filing its ANDA, each party infringed the newly-issued patent related to a method of treatment using Xywav. The suits seek orders that the effective date of FDA approval of each defendant's application shall be a date no earlier than the expiration of the newly-issued patent.

Epidiolex Patent Litigation

In November and December 2022, we received notices from the Epidiolex ANDA Filers, that they have each filed with FDA an ANDA for a generic version of Epidiolex (cannabidiol) oral solution. As of the date of this filing, we are not aware of other ANDA filers. The notices from the Epidiolex ANDA Filers each included a "paragraph IV certification" with respect to certain of our patents listed in FDA's Orange Book for Epidiolex on the date of the receipt of the notice. The listed patents relate generally to the composition and method of use of Epidiolex, and methods of treatment using Epidiolex. A paragraph IV certification is a certification by a generic applicant that alleges that patents covering the branded product are invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product.

On January 3, 2023, we filed a patent infringement suit against the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey. The complaint alleges that by filing their ANDAs, the Epidiolex ANDA Filers have infringed certain of our Orange Book listed patents, and seeks an order that the effective date of FDA approval of the ANDAs shall be a date no earlier than the expiration of the last to expire of the asserted patents. As a result of this lawsuit, we expect that a stay of approval of up to 30 months will be imposed by FDA on the Epidiolex ANDA Filers' ANDAs.

From March 2023 through May 2023, we received the Epidiolex ANDA Filers' answers to the complaint. The answers include defenses and counterclaims asserting that the Epidiolex ANDA Filers' products, if launched, would not infringe our patents, that our patents are invalid and, in one instance, counterclaims related to allegations of inequitable conduct and improper listing of patents in the Orange Book. On May 25, 2023, we filed a motion to dismiss certain of the counterclaims. On January 11, 2024, the Court issued an order granting in part and denying in part our motion to dismiss. On September 20, 2024, the Court held a claim construction hearing relating to disputed terms in the asserted patents. The Court has not yet issued a decision on the claim construction disputes.

The Court in the Epidiolex Patent Litigation scheduled trial for September 2025.

In June and July 2023, we received notice from certain of the Epidiolex ANDA Filers that they had each filed a paragraph IV certification regarding a newly-issued patent listed in the Orange Book for Epidiolex. On July 21, 2023, we filed an additional lawsuit against all of the Epidiolex ANDA Filers in the United States District Court for the District of New Jersey alleging that, by filing its ANDA, each Epidiolex ANDA Filer infringed the newly-issued patent related to a method of treatment using Epidiolex. The suit seeks an order that the effective date of FDA approval of each Epidiolex ANDA Filer's application shall be a date no earlier than the expiration of the newly-issued patent.

In September and October 2023, we received notice from certain of the Epidiolex ANDA Filers that they had each filed a paragraph IV certification regarding one or more newly-issued patents listed in the Orange Book for Epidiolex. On December 15, 2023, we filed an additional lawsuit against seven of the original Epidiolex ANDA Filers with whom we have not previously settled. We filed this lawsuit in the United States District Court for the District of New Jersey alleging that, by filing its ANDA, each Epidiolex ANDA Filer infringed the newly-issued patents related to methods of treatment using

Epidiolex. The suit seeks an order that the effective date of FDA approval of each Epidiolex ANDA Filer's application shall be a date no earlier than the expiration of the newly-issued patents.

In March and April 2024, we received notice from certain of the Epidiolex ANDA Filers that they had each filed a paragraph IV certification regarding one or more newly-issued patents listed in the Orange Book for Epidiolex. On July 3, 2024, we filed an additional lawsuit against six of the original Epidiolex ANDA Filers with whom we had not previously settled. We filed this lawsuit in the United States District Court for the District of New Jersey alleging that, by filing its ANDA, each Epidiolex ANDA Filer infringed the newly-issued patents related to methods of treatment using Epidiolex. The suit seeks an order that the effective date of FDA approval of each Epidiolex ANDA Filer's application shall be a date no earlier than the expiration of the newly-issued patents.

From October 2023 through January 2025, we entered into settlement agreements with each of the Epidiolex ANDA Filers that resolved our patent litigation with them related to Epidiolex. Under the settlement agreements, we granted each of the Epidiolex ANDA Filers a license to manufacture, market, and sell its own generic version of Epidiolex beginning in the very late 2030s, or earlier under certain circumstances, including but not limited to the launch of another generic Epidiolex product or a final decision that all unexpired claims of the Epidiolex patents are not infringed, or are invalid and/or unenforceable.

Zepzelca Patent Litigation

In July and August 2024, we received notices from the Zepzelca ANDA Filers that they have each filed with FDA an ANDA for a generic version of Zepzelca (lurbinectedin). As of the date of this filing, we are not aware of other ANDA filers. The notices from the Zepzelca ANDA Filers each included a paragraph IV certification with respect to a patent listed in the Orange Book for Zepzelca on the date of the receipt of the notice. The listed patent relates to the drug substance, drug product and approved use of Zepzelca. Jazz is the exclusive licensee to this Zepzelca patent pursuant to an agreement with PharmaMar. A paragraph IV certification is a certification by a generic applicant that alleges that the patent covering the branded product is invalid, unenforceable, and/or will not be infringed by the manufacture, use or sale of the generic product.

On September 11, 2024, we and PharmaMar filed a patent infringement suit against the Zepzelca ANDA Filers in the United States District Court for the District of New Jersey. The complaint alleges that by filing their ANDAs, the Zepzelca ANDA Filers have infringed the Orange Book listed patent for Zepzelca, and seeks an order that the effective date of FDA approval of the ANDAs shall be a date no earlier than the expiration of the asserted patent.

In December 2024, we received the Zepzelca ANDA Filers' answers to the complaint. The answers include defenses and counterclaims asserting that the Zepzelca ANDA Filers' products, if launched, would not infringe our patents and that our patents are invalid. No trial date has been set in this matter.

On September 12, 2024, we and PharmaMar filed a patent infringement suit against RK Pharma, in the United States District Court for the District of Delaware. The complaint alleges that by filing its ANDA, RK Pharma has infringed the Orange Book listed patent for Zepzelca, and seeks an order that the effective date of FDA approval of RK Pharma's ANDA shall be no earlier than the expiration of the asserted patent. On November 13, 2024, we voluntarily dismissed this action against RK Pharma in the United States District Court for the District of Delaware. RK Pharma remains a defendant in the litigation referenced above in the United States District Court for the District of New Jersey.

MSP Litigation

On April 3, 2023, MSP filed a class action lawsuit on behalf itself and others similarly situated against the Defendants in the United States District Court for the Northern District of California. The MSP complaint alleges that the Defendants conspired to increase the price and quantity dispensed of Xyrem and Prialta, in violation of the Racketeer Influenced and Corrupt Organizations Act and several state laws. The allegations relate generally to the conduct at issue in the investigation conducted by the United States Department of Justice from 2016-2019, involving the Company's contributions to certain charitable foundations. MSP seeks monetary damages, restitution, disgorgement, and a declaration that the conduct alleged is unlawful.

On July 25, 2023, we and certain other defendants filed motions to dismiss MSP's complaint, which the Court granted on December 12, 2023. On January 5, 2024, the MSP filed an amended complaint. On February 20, 2024, we filed a motion to dismiss MSP's amended complaint. The Court scheduled a hearing on the motion for June 13, 2024. On June 21, 2024, the Court cancelled the hearing. On July 22, 2024, the Court granted the motion. The Court set a deadline of August 12, 2024, to file a second amended complaint. On August 12, 2024, MSP voluntarily dismissed its complaint.

FDA Litigation

On June 22, 2023, we filed a complaint in the United States District Court for the District of Columbia seeking a declaration that FDA's approval on May 1, 2023, of the NDA for Avadel's Lumryz was unlawful. In the complaint, we alleged that FDA acted outside its authority under the Orphan Drug Act, when, despite ODE protecting Jazz's low-sodium oxybate

product Xywav, FDA approved the Lumryz NDA and granted Lumryz ODE based on FDA's finding that Lumryz makes a major contribution to patient care and is therefore clinically superior to Xywav and Xyrem. Jazz further alleged that, in doing so, FDA failed to follow its own regulations, failed to follow established agency policy without providing a reasoned explanation for the departure, reversed prior decisions by its own staff and experts without a reasoned explanation, and disregarded the relevant scientific literature and data. The complaint, filed pursuant to the Administrative Procedure Act, asked the Court to vacate and set aside FDA's approval of the Lumryz NDA and sought a declaration that FDA's approval of the Lumryz NDA was arbitrary, capricious, an abuse of discretion and otherwise not in accordance with law and that approval of the Lumryz NDA was in excess of FDA's statutory authority and was made without observance of procedure required by law.

On September 15, 2023, we filed a motion for summary judgment. On October 20, 2023, Avadel and FDA filed cross motions for summary judgment. Oral argument on these motions was held on May 10, 2024 and on October 30, 2024, the District Court issued an order denying Jazz's motion for summary judgment and granting Avadel's and FDA's cross-motions for summary judgment. Jazz respectfully disagrees with the Court's decision and is appealing the matter to the United States Court of Appeals for the District of Columbia Circuit. We filed our opening appeal brief on January 31, 2025. No argument date has been set.

Qui tam matter

In July 2022, we received a subpoena from the USAO for the District of Massachusetts requesting documents related to Xyrem and U.S. Patent No. 8,772,306 ("Method of Administration of Gamma Hydroxybutyrate with Monocarboxylate Transporters"), product labeling changes for Xyrem, communications with FDA and the USPTO, pricing of Xyrem, and other related documents. On July 18, 2024, the United States District Court for the District of Massachusetts unsealed a qui tam whistleblower lawsuit underlying the USAO's subpoena, captioned 1:21-cv-10891-PBS and originally filed under seal on May 27, 2021. The public docket in this matter indicates that on May 24 and June 7, 2024, respectively, the United States and a number of states named in the whistleblower complaint declined to intervene in this matter. As such, private whistleblower litigation will proceed in the United States District Court for the District of Massachusetts. The Court set a deadline of September 1, 2024, for the plaintiff to file an amended complaint, and December 2, 2024, for us to file a motion to dismiss the amended complaint. The plaintiff filed the amended complaint on September 1, 2024. We filed our motion to dismiss on December 2, 2024. The Court scheduled a hearing on the motion to dismiss for April 2, 2025.

From time to time, we are involved in legal proceedings arising in the ordinary course of business. We believe there is no other litigation pending that could have, individually or in the aggregate, a material adverse effect on our results of operations or financial condition.

14. Shareholders' Equity

Share Repurchase Program

In July 2024, our board of directors authorized the New Repurchase Program, to repurchase ordinary shares having an aggregate purchase price of \$500.0 million, exclusive of any brokerage commissions. Under the New Repurchase Program, which has no expiration date, we may repurchase ordinary shares from time to time by any methods and/or structures permitted by applicable law. The timing and amount of repurchases will depend on a variety of factors, including the price of our ordinary shares, alternative investment opportunities, restrictions under the Amended Credit Agreement and the indenture for our Secured Notes, corporate and regulatory requirements and market conditions. The New Repurchase Program may be modified, suspended or discontinued at any time without our prior notice. The New Repurchase Program replaces and supersedes the Old Repurchase Program, a share repurchase program to repurchase ordinary shares having an aggregate purchase price of \$1.5 billion, exclusive of any brokerage commissions. In 2024, we spent a total of \$150.0 million to repurchase 1.4 million of our ordinary shares, all under the New Repurchase Program, at a purchase price, including commissions, of \$109.32 per share and \$161.4 million to repurchase 1.5 million of our ordinary shares, all under the Old Repurchase Program, at a purchase price, including commissions, of \$110.75 per share. The repurchases made under the New Share Repurchase Program in 2024 were effected in privately negotiated transactions with or through one of the initial purchasers of the 2030 Notes concurrently with the pricing of the offering of the 2030 Notes. In 2023, we spent a total of \$269.8 million to purchase 2.1 million of our ordinary shares under the Old Repurchase Program at an average total purchase price, including commissions, of \$126.65 per share. All ordinary shares repurchased were cancelled. As of December 31, 2024, the remaining amount authorized for repurchases under the New Repurchase Program was \$350.0 million, exclusive of any brokerage commissions.

Authorized But Unissued Ordinary Shares

We had reserved the following shares of authorized but unissued ordinary shares (in thousands):

	December 31,	
	2024	2023
2011 Equity Incentive Plan	22,056	22,855
2007 Employee Stock Purchase Plan	3,701	3,913
GW Incentive Plans	1,408	1,570
Amended and Restated 2007 Non-Employee Directors Stock Award Plan	677	714
Total	27,842	29,052

Dividends

In 2024 and 2023, we did not declare or pay cash dividends on our common equity. Under Irish law, dividends may only be paid, and share repurchases and redemptions must generally be funded only out of, “distributable reserves.” In addition, the terms of the Amended Credit Agreement restrict our ability to make certain restricted payments, including dividends and other distributions by us in respect of our ordinary shares, subject to, among other exceptions, (1) a general exception for dividends and other restricted payments not to exceed in the aggregate the greater of \$350 million and 3.5% of consolidated total assets (as defined in the Amended Credit Agreement) when made, and (2) an exception that allows for dividends and other restricted payments equal to an amount tied to our financial performance, so long as no default or event of default shall have occurred and is continuing under the Amended Credit Agreement and the total net leverage ratio (as defined in in the Amended Credit Agreement) on a pro forma basis does not exceed 5:1, and (3) an exception that allows for additional dividends and other restricted payments, so long as no default or event of default shall have occurred and is continuing under the Amended Credit Agreement and the total net total leverage ratio (as defined in the Amended Credit Agreement) on a pro forma basis is not greater than 4:1. Any future determination as to the payment of dividends will, subject to Irish legal requirements, be at the sole discretion of our board of directors and will depend on our consolidated financial condition, results of operations, capital requirements, compliance with the terms of the Amended Credit Agreement or other future borrowing arrangements, and other factors our board of directors deems relevant.

15. Comprehensive Income (Loss)

Comprehensive income (loss) includes net income (loss) and all changes in shareholders’ equity during a period, except for those changes resulting from investments by shareholders or distributions to shareholders.

Accumulated Other Comprehensive Loss

The components of accumulated other comprehensive loss as of December 31, 2024 and 2023 were as follows (in thousands):

	Net Unrealized Gain From Hedging Activities	Foreign Currency Translation Adjustments	Total Accumulated Other Comprehensive Loss
Balance at December 31, 2023	\$ 235	\$ (842,382)	\$ (842,147)
Other comprehensive income (loss) before reclassifications	5,298	(106,025)	(100,727)
Amounts reclassified from accumulated other comprehensive loss	(4,793)	—	(4,793)
Other comprehensive income (loss), net	505	(106,025)	(105,520)
Balance at December 31, 2024	\$ 740	\$ (948,407)	\$ (947,667)

In 2024, other comprehensive income (loss) primarily reflects foreign currency translation adjustments due to the weakening of sterling and the euro against the U.S. dollar.

16. Net Income (Loss) per Ordinary Share

Basic net income (loss) per ordinary share is based on the weighted-average number of ordinary shares outstanding. Diluted net income (loss) per ordinary share is based on the weighted-average number of ordinary shares outstanding and potentially dilutive ordinary shares outstanding.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS—(Continued)

Basic and diluted net income (loss) per ordinary share were computed as follows (in thousands, except per share amounts):

	Year Ended December 31,		
	2024	2023	2022
Numerator:			
Net income (loss)	\$ 560,120	\$ 414,832	\$ (224,060)
Effect of interest on assumed conversions of the 2026 Notes and the 2024 Notes, net of tax	10,762	24,876	—
Net income (loss) for dilutive net income (loss) per ordinary share	<u>\$ 570,882</u>	<u>\$ 439,708</u>	<u>\$ (224,060)</u>
Denominator:			
Weighted-average ordinary shares used in per share calculations - basic	61,838	63,291	62,539
Dilutive effect of the 2026 Notes and the 2024 Notes	3,540	8,016	—
Dilutive effect of employee equity incentive and purchase plans	629	759	—
Weighted-average ordinary shares used in per share calculations - diluted	<u>66,007</u>	<u>72,066</u>	<u>62,539</u>
Net income (loss) per ordinary share:			
Basic	<u>\$ 9.06</u>	<u>\$ 6.55</u>	<u>\$ (3.58)</u>
Diluted	<u>\$ 8.65</u>	<u>\$ 6.10</u>	<u>\$ (3.58)</u>

Potentially dilutive ordinary shares from our employee equity incentive and purchase plans are determined by applying the treasury stock method to the assumed vesting of outstanding RSUs and PRSUs, the assumed exercise of share options and the assumed issuance of ordinary shares under our ESPP.

On January 1, 2022, we adopted ASU No. 2020-06, “Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging— Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity” on a modified retrospective basis, which requires the use of the if-converted method to calculate potentially dilutive ordinary shares for convertible instruments.

In August 2023, we made an irrevocable election to fix the settlement method for exchanges of the 2024 Notes to a combination of cash and ordinary shares of the Company with a specified cash amount per \$1,000 principal amount of the 2024 Notes of \$1,000. As a result of the election, an exchanging holder will receive (i) up to \$1,000 in cash per \$1,000 principal amount of 2024 Notes exchanged and (ii) cash, ordinary shares, or any combination thereof, at our election, in respect of the remainder, if any, of its exchange obligation in excess of \$1,000 per \$1,000 principal amount of 2024 Notes exchanged. As a result, the assumed issuance of ordinary shares upon exchange of the 2024 Notes has only been included in the calculation of diluted net income per ordinary share in 2023 up to the date the irrevocable election was made.

In July 2024, we irrevocably elected to fix the settlement method for exchanges of the 2026 Notes to a combination of cash and ordinary shares of Jazz Pharmaceuticals plc with a specified cash amount per \$1,000 principal amount of 2026 Notes exchanged equal to or in excess of \$1,000. As a result of the election, an exchanging holder will receive (i) up to \$1,000 in cash per \$1,000 principal amount of 2026 Notes exchanged and (ii) cash, ordinary shares, or any combination thereof, at our election, in respect of the remainder, if any, of its exchange obligation in excess of \$1,000 per \$1,000 principal amount of 2026 Notes exchanged. As a result, the assumed issuance of ordinary shares upon exchange of the 2026 Notes has only been included in the calculation of diluted net income per ordinary share in 2024, up to the date the irrevocable election was made.

The potential issue of ordinary shares upon exchange of the 2026 Notes and the 2024 Notes was anti-dilutive and had no impact on diluted net loss per ordinary share for 2022.

For the 2030 Notes, we are required to settle the principal amount in cash and have the option to settle the conversion feature for the amount above the conversion price, or the conversion spread, in cash, ordinary shares or a combination of cash and ordinary shares. The conversion spread will have a dilutive impact on diluted net income per ordinary share when the average market price of our ordinary shares for a given period exceeds the conversion price of the 2030 Notes. For the year ended December 31, 2024, the 2030 Notes have been excluded from the computation of diluted net income per ordinary share, as the effect would be anti-dilutive since the conversion price of the 2030 Notes exceeded the average market price of our ordinary shares for the year ended December 31, 2024.

The following table represents the weighted-average ordinary shares that were excluded from the computation of diluted net income (loss) per ordinary share for the years presented because including them would have an anti-dilutive effect (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Employee equity incentive and purchase plans	4,074	2,973	2,751
2026 Notes and 2024 Notes	—	—	9,044

17. Segment and Other Information

Our operating segment is reported in a manner consistent with the internal reporting provided to the CODM. Our CODM has been identified as our chief executive officer. We have determined that we operate in one business segment, which is the identification, development and commercialization of meaningful pharmaceutical products that address unmet medical needs. The CODM assesses performance and decides how to allocate resources for the segment based on net income (loss) and measure of segment assets which is reported on the Consolidated Statements of Income (Loss) and Consolidated Balance Sheet.

The following table presents total long-lived assets by location (in thousands):

	December 31,	
	2024	2023
Ireland	\$ 85,703	\$ 68,201
United Kingdom	77,741	80,293
United States	33,724	59,440
Italy	21,931	20,942
Other	7,896	6,110
Total long-lived assets (1)	<u>\$ 226,995</u>	<u>\$ 234,986</u>

(1) Long-lived assets consist of property, plant and equipment and operating lease assets.

18. Revenues

The following table presents a summary of total revenues (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Xywav	\$ 1,473,202	\$ 1,272,977	\$ 958,425
Xyrem	233,816	569,730	1,020,453
Epidiolex/Epidyolex	972,423	845,468	736,398
Sativex	18,877	19,668	16,825
Sunosi ¹	—	—	28,844
Total Neuroscience	2,698,318	2,707,843	2,760,945
Rylaze/Enrylaze	410,846	394,226	281,659
Zepzelca	320,318	289,533	269,912
Defitelio/defibrotide	216,565	184,000	194,290
Vyxeos	162,595	147,495	127,980
Ziihera	1,051	—	—
Total Oncology	1,111,375	1,015,254	873,841
Other	11,471	13,846	6,643
Product sales, net	3,821,164	3,736,943	3,641,429
High-sodium oxybate AG royalty revenue	217,575	75,918	—
Other royalty and contract revenues	30,211	21,343	17,945
Total revenues	\$ 4,068,950	\$ 3,834,204	\$ 3,659,374

(1) Divestiture of Sunosi U.S. was completed in May 2022.

The following table presents a summary of total revenues attributed to geographic sources (in thousands):

	Year Ended December 31,		
	2024	2023	2022
United States	\$ 3,660,109	\$ 3,489,977	\$ 3,370,379
Europe	312,706	269,243	239,638
All other	96,135	74,984	49,357
Total revenues	\$ 4,068,950	\$ 3,834,204	\$ 3,659,374

The following table presents a summary of the percentage of total revenues from customers that represented more than 10% of our total revenues:

	Year Ended December 31,		
	2024	2023	2022
ESSDS	42 %	48 %	56 %
McKesson	12 %	11 %	11 %

Financing and payment

Our payment terms vary by the type and location of our customer, but payment is generally required in a term ranging from 30 to 65 days.

19. Share-Based Compensation**GW Incentive Plans**

On May 5, 2021, Jazz Pharmaceuticals plc acquired the entire issued share capital of GW. In connection with the GW Acquisition, we assumed the GW Incentive Plans. The terms of the GW Incentive Plans provide for the grant of stock options, stock appreciation rights, RSUs, other stock awards, and performance awards that may be settled in cash, shares, or other

property. Ordinary shares granted to employees in exchange for GW ADS, in connection with the GW Acquisition, vest ratably over service periods of two years, while all post-acquisition grants vest ratably over service periods of four years and expire no more than 10 years after the date of grant. As of December 31, 2024, a total of 1,864,475 of our ordinary shares had been authorized for issuance under the GW Incentive Plans.

2011 Equity Incentive Plan

In connection with the Azur Merger, Jazz Pharmaceuticals, Inc.'s board of directors adopted the 2011 Plan in October 2011, and its stockholders approved the 2011 Plan at the special meeting of the stockholders held in December 2011. The 2011 Plan became effective immediately before the consummation of the Azur Merger and was assumed and adopted by us upon the consummation of the Azur Merger. The terms of the 2011 Plan provide for the grant of stock options, stock appreciation rights, RSUs, other stock awards, and performance awards that may be settled in cash, shares, or other property. All outstanding grants under the 2011 Plan were granted to employees and vest ratably over service periods of four years and expire no more than 10 years after the date of grant. As of December 31, 2024, a total of 34,836,988 of our ordinary shares had been authorized for issuance under the 2011 Plan.

2007 Employee Stock Purchase Plan

In 2007, Jazz Pharmaceuticals, Inc.'s employees became eligible to participate in the ESPP. The ESPP was amended and restated by Jazz Pharmaceuticals, Inc.'s board of directors in October 2011 and approved by its stockholders in December 2011. The amended and restated ESPP became effective immediately prior to the effective time of the Azur Merger and was assumed by us upon the consummation of the Azur Merger. The amended and restated ESPP allows our eligible employee participants (including employees of any parent or subsidiary company if our board of directors designates such company as eligible to participate) to purchase our ordinary shares at a discount of 15% through payroll deductions. The ESPP consists of a fixed offering period of 24 months with four purchase periods within each offering period. The number of shares available for issuance under our ESPP during any six-month purchase period is 175,000 shares. As of December 31, 2024, a total of 7,029,250 of our ordinary shares had been authorized for issuance under the ESPP.

Amended and Restated 2007 Non-Employee Directors Stock Award Plan

The Amended and Restated 2007 Directors Award Plan, which was initially adopted by the Jazz Pharmaceuticals, Inc. board of directors and approved by the Jazz Pharmaceuticals, Inc. stockholders in connection with its initial public offering, was continued and assumed by us upon the consummation of the Azur Merger. Until October 2011, the 2007 Directors Award Plan provided for the automatic grant of stock options to purchase shares of Jazz Pharmaceuticals, Inc.'s common stock to its non-employee directors initially at the time any individual first became a non-employee director, which vest over three years, and then annually over their period of service on its board of directors, which vest over one year. On October 24, 2011, Jazz Pharmaceuticals, Inc.'s board of directors amended the 2007 Directors Award Plan to eliminate all future initial and annual automatic grants so that future automatic grants would not be made that would be subject to the excise tax imposed by the Internal Revenue Code in connection with the Azur Merger. Accordingly, all future stock option grants under the 2007 Directors Award Plan will be at the discretion of our board of directors. Since the Azur Merger, all of the new grants under the 2007 Directors Award Plan were granted to non-employee directors and vest ratably over service periods of one to three years and expire no more than 10 years after the date of grant. In August 2016, our shareholders approved our proposal to expand the types of stock awards that may be granted to our non-employee directors under the 2007 Directors Award Plan and eliminate the final automatic share reserve increase under the 2007 Directors Award Plan that was scheduled to occur on January 1, 2017. In July 2020, our shareholders approved our proposal to increase the number of ordinary shares authorized for issuance under the 2007 Directors Award Plan by 500,000 shares. As of December 31, 2024, a total of 1,403,938 of our ordinary shares had been authorized for issuance under the 2007 Directors Award Plan.

Share-Based Compensation

Share-based compensation expense related to RSUs, PRSUs, grants under our ESPP and share options was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Selling, general and administrative	\$ 158,570	\$ 146,942	\$ 151,986
Research and development	74,673	64,847	57,522
Cost of product sales	14,802	15,052	12,488
Total share-based compensation expense, pre-tax	248,045	226,841	221,996
Income tax benefit from share-based compensation expense	(40,552)	(40,015)	(41,058)
Total share-based compensation expense, net of tax	\$ 207,493	\$ 186,826	\$ 180,938

We recognized income tax benefits related to share option exercises of \$0.3 million, \$1.9 million and \$8.0 million in 2024, 2023 and 2022, respectively.

Restricted Stock Units

In 2024, 2023 and 2022, we granted RSUs covering an equal number of our ordinary shares to employees with a weighted-average grant date fair value of \$118.41, \$144.65 and \$152.08, respectively. The fair value of RSUs is determined on the date of grant based on the market price of our ordinary shares as of that date. The fair value of RSUs is recognized as an expense ratably over the vesting period of four years. In 2024, 2023 and 2022, 1,341,000, 1,094,000 and 910,000 RSUs were released, respectively, with 892,000, 735,000 and 610,000 ordinary shares issued, respectively, and 449,000, 359,000 and 300,000 ordinary shares withheld for tax purposes, respectively. The total fair value of shares vested was \$156.0 million, \$155.5 million and \$138.1 million during 2024, 2023 and 2022, respectively.

As of December 31, 2024, total compensation cost not yet recognized related to unvested RSUs was \$308.9 million, which is expected to be recognized over a weighted-average period of 2.4 years.

The following table summarizes information as of December 31, 2024 and activity during 2024 related to our RSUs:

	Number of RSUs (In thousands)	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2024	3,563	\$ 148.79		
RSUs granted	2,260	118.41		
RSUs released	(1,341)	147.14		
RSUs forfeited	(449)	137.25		
Outstanding at December 31, 2024	4,033	\$ 133.60	1.3	\$ 496,716

Performance-Based Restricted Stock Units

The Compensation & Management Development Committee of our board of directors and, in the case of our Chief Executive Officer, the independent members of our board of directors, approved awards of PRSUs to certain employees of the Company, subject to vesting on the achievement of certain commercial and pipeline performance criteria to be assessed over a performance period from the date of the grant to December 31, 2024, December 31, 2025 and December 31, 2026, respectively. The number of shares that vest is determined based on the Company's achievement with respect to the performance criteria. For PRSUs granted prior to 2024, the amount of shares that vest will be subject to adjustment based on the application of a relative TSR modifier. For PRSUs granted in 2024, the relative TSR represents one of the performance metrics. In both cases, the number of shares that may be earned ranges between 0% and 200% of the target number of PRSUs granted.

The following table summarizes information as of December 31, 2024 and activity during 2024 related to our PRSUs:

	Number of PRSUs (In thousands)	Weighted-Average Grant-Date Fair Value	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2024	664	\$ 173.30		
PRSUs granted	377	131.04		
PRSUs released	(124)	190.81		
PRSUs forfeited	(136)	169.40		
Outstanding at December 31, 2024	781	\$ 150.82	1.1	\$ 96,218

As of December 31, 2024, total compensation cost not yet recognized related to unvested PRSUs was \$37.3 million, which is expected to be recognized over a weighted-average period of 1.1 years.

As the PRSUs granted in each year are subject to a market condition, the grant date fair value for such PRSUs was based on a Monte Carlo simulation model. In 2024, 2023 and 2022, we granted PRSUs to employees with a weighted-average grant date fair value of \$131.04, \$156.91 and \$178.78, respectively. The Company evaluated the performance targets in the context of its current long-range financial plan and its product candidate development pipeline and recognized compensation expense based on the probable number of awards that will ultimately vest. In 2024, 124,000 PRSUs were released, with 80,000 ordinary shares issued and 44,000 ordinary shares withheld for tax purposes. The total fair value of shares vested was \$14.8 million during 2024.

Share Options

There were no share options granted in 2024, 2023 and 2022.

The following table summarizes information as of December 31, 2024 and activity during 2024 related to our share option plans:

	Shares Subject to Outstanding Options (In thousands)	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2024	2,716	\$ 141.55		
Options exercised	(14)	115.81		
Options forfeited	(8)	163.35		
Options expired	(536)	148.99		
Outstanding at December 31, 2024	2,158	\$ 139.79	3.2	\$ 3,562
Vested and expected to vest at December 31, 2024	2,158	\$ 139.79	3.2	\$ 3,562
Exercisable at December 31, 2024	2,158	\$ 139.79	3.2	\$ 3,562

Aggregate intrinsic value shown in the table above is equal to the difference between the exercise price of the underlying share options and the fair value of our ordinary shares for share options that were in the money. The aggregate intrinsic value changes based on the fair market value of our ordinary shares. The aggregate intrinsic value of share options exercised was \$0.2 million, \$6.3 million and \$34.8 million during 2024, 2023 and 2022, respectively. We issued new ordinary shares upon exercise of share options.

As of December 31, 2024, total compensation cost not yet recognized related to unvested share options was \$0.1 million, which is expected to be recognized over a weighted-average period of 0.1 years.

As of December 31, 2024, total compensation cost not yet recognized related to grants under the ESPP was \$7.6 million, which is expected to be recognized over a weighted-average period of 1.1 years.

Nominal Strike Price Options

During the second quarter of 2021, we issued nominal strike price options to replace certain unvested GW awards, in connection with the GW Acquisition, with a weighted-average grant date fair value of \$170.82. The fair value of nominal strike price options was determined on the date of the grant based on the market price of our ordinary shares as of that date.

The following table summarizes information as of December 31, 2024 and activity during 2024 related to our nominal strike price options:

	Shares Subject to Outstanding Options (In thousands)	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (Years)	Aggregate Intrinsic Value (In thousands)
Outstanding at January 1, 2024	27	\$ 0.02		
Options exercised	(8)	0.02		
Outstanding at December 31, 2024	19	\$ 0.02	6.0	\$ 2,374
Vested and expected to vest at December 31, 2024	19	\$ 0.02	6.0	\$ 2,374
Exercisable at December 31, 2024	19	\$ 0.02	6.0	\$ 2,374

The aggregate intrinsic value of nominal strike price options exercised was \$0.9 million, \$3.9 million and \$8.4 million during 2024, 2023 and 2022, respectively. We issued new ordinary shares upon exercise of nominal strike price options.

20. Employee Benefit Plans

We maintain a qualified 401(k) savings plan, in which all U.S. based employees are eligible to participate, provided they meet the requirements of the plan. We match certain employee contributions under the 401(k) savings plan and for the years ended December 31, 2024, 2023 and 2022 we recorded expense of \$16.4 million, \$13.4 million and \$10.6 million, respectively, related to this plan.

We also operate a number of defined contribution retirement plans for certain non-U.S. based employees. Expenses related to contributions to such plans for the years ended December 31, 2024, 2023 and 2022 were \$15.2 million, \$14.0 million and \$14.6 million, respectively.

21. Income Taxes

The components of income (loss) before income tax benefit and equity in loss of investees were as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Ireland	\$ 497,860	\$ 449,214	\$ (50,311)
United Kingdom	(411,356)	(643,096)	(963,598)
United States	29,594	(6,056)	224,453
Other	354,253	497,867	416,672
Total	\$ 470,351	\$ 297,929	\$ (372,784)

The following table sets forth the details of income tax benefit (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Current			
Ireland	\$ 97,680	\$ 77,343	\$ 61,550
United Kingdom	207	7,726	1,454
United States	22,065	20,803	37,823
Other	(3,054)	34,433	32,779
Total current tax expense	116,898	140,305	133,606
Deferred, exclusive of other components below			
Ireland	(20,022)	(10,919)	(62,011)
United Kingdom	(114,600)	(150,506)	(193,219)
United States	(63,162)	(89,246)	(9,086)
Other	(11,481)	(8,990)	(11,144)
Total deferred, exclusive of other components	(209,265)	(259,661)	(275,460)
Deferred, change in tax rates			
United Kingdom	—	268	(16,990)
United States	955	(824)	201
Other	(17)	—	(2)
Total deferred, change in tax rates	938	(556)	(16,791)
Total deferred tax benefit	(208,327)	(260,217)	(292,251)
Total income tax benefit	\$ (91,429)	\$ (119,912)	\$ (158,645)

Our income tax benefit was \$91.4 million, \$119.9 million and \$158.6 million in 2024, 2023 and 2022, respectively, relating to tax arising on income or losses in Ireland, the U.K., the U.S. and certain other foreign jurisdictions, offset by deductions on subsidiary equity, patent box benefits, foreign derived intangible income benefits and originating tax credits. Our income tax benefit in 2024 decreased compared to 2023 primarily due to the change in income mix across jurisdictions, partially offset by patent box benefits. Our income tax benefit in 2023 decreased compared to 2022 primarily due to pretax losses from payments for acquired IPR&D made in 2022 and the 2022 impairment of our acquired IPR&D asset as a result of the decision to discontinue our nabiximols program, partially offset by the change in income mix across jurisdictions.

The reconciliation between income tax expense (benefit) at the Irish statutory trading income tax rate of 12.5 percent, the jurisdiction of tax domicile of Jazz Pharmaceuticals, applied to income before the income tax expense (benefit) and equity in loss of investees and our reported income tax benefit was as follows (in thousands):

	Year Ended December 31,		
	2024	2023	2022
Income tax expense (benefit) at the statutory income tax rate	\$ 58,794	\$ 37,241	\$ (46,598)
Change in valuation allowance	201,996	75,081	95,051
Deduction on subsidiary equity	(180,460)	(153,655)	(158,488)
Change in estimates	(106,007)	(5,472)	(14,065)
Patent box incentive benefit	(65,413)	(13,862)	(6,203)
Research and other tax credits	(65,255)	(49,900)	(27,976)
Foreign derived intangible income benefit	(39,470)	(42,400)	(29,541)
Foreign income tax rate differential	38,346	(7,763)	5,863
Non-deductible financing costs	22,437	15,705	4,504
Tax deficiencies/(excess tax benefits) from share-based compensation	18,074	3,959	(1,690)
Non-deductible compensation	10,889	14,092	13,505
Change in unrecognized tax benefits	9,767	(12,612)	5,029
Change in tax rate	938	(605)	(16,790)
Non-deductible facility expense	22	16,618	8,093
Non-deductible royalty expense	—	—	6,274
Other	3,913	3,661	4,387
Reported income tax benefit	<u>\$ (91,429)</u>	<u>\$ (119,912)</u>	<u>\$ (158,645)</u>

The 2024 patent box incentive benefit above includes a non-recurring benefit of \$40.9 million related to a claim for benefits in Italy in respect of tax years 2020 to 2023. The 2024 change in estimates above includes a benefit of \$103.3 million that is fully offset by a related change in valuation allowance, resulting in a net nil impact to our income tax benefit.

Significant components of our net deferred tax assets (liabilities) were as follows (in thousands):

	December 31,	
	2024	2023
Deferred tax assets:		
Deduction on subsidiary equity carryforwards	\$ 393,960	\$ 212,015
Operating loss carryforwards	307,413	296,490
Capitalized research and development	295,779	201,186
Intangible assets	243,391	238,062
Tax credit carryforwards	127,483	142,854
Accrued liabilities	115,290	128,948
Share-based compensation	47,486	48,403
Indirect effects of unrecognized tax benefits	35,000	40,811
Other	15,714	19,340
Total deferred tax assets	1,581,516	1,328,109
Valuation allowance	(509,190)	(312,340)
Deferred tax assets, net of valuation allowance	1,072,326	1,015,769
Deferred tax liabilities:		
Intangible assets	(1,130,485)	(1,290,425)
Inventories	(47,802)	(81,995)
Other	(10,530)	(13,221)
Total deferred tax liabilities	(1,188,817)	(1,385,641)
Net deferred tax liabilities	<u>\$ (116,491)</u>	<u>\$ (369,872)</u>

The net change in valuation allowance was an increase of \$196.9 million, \$77.6 million, and \$80.5 million in 2024, 2023 and 2022, respectively.

The following table summarizes the presentation of deferred tax assets and liabilities (in thousands):

	December 31,	
	2024	2023
Deferred tax assets	\$ 560,245	\$ 477,834
Deferred tax liabilities	(676,736)	(847,706)
Net deferred tax liabilities	<u>\$ (116,491)</u>	<u>\$ (369,872)</u>

As of December 31, 2024, we had NOL and tax credit carryforwards for U.S. federal income tax purposes of \$11.0 million and \$20.5 million, respectively, available to reduce future income subject to income taxes. The U.S. federal NOL carryforwards will expire, if not utilized, in the tax years 2025 to 2033 and the U.S. federal tax credits will expire, if not utilized, in the tax years 2027 to 2044. In addition, we had \$4.9 million of NOL carryforwards and \$5.8 million of tax credit carryforwards as of December 31, 2024 available to reduce future taxable income for U.S. state income tax purposes. The U.S. state NOL carryforwards will expire, if not utilized, in the tax years 2025 to 2034. As of December 31, 2024, there were NOL and other carryforwards for income tax purposes of \$1,125.6 million, \$790.3 million and \$374.8 million available to reduce future income subject to income taxes in Malta, the United Kingdom and Ireland respectively. The NOLs and other carryforwards generated in Malta, the United Kingdom and Ireland have no expiration date. We also had foreign tax credit carryforwards in Ireland, as of December 31, 2024, of \$100.9 million, which may only be utilized against certain sources of income. The foreign tax credit carryforwards have no expiration date.

Utilization of certain of our NOL and tax credit carryforwards in the U.S. is subject to an annual limitation due to the ownership change limitations provided by Sections 382 and 383 of the Internal Revenue Code and similar state provisions. Such an annual limitation may result in the expiration of certain NOLs and tax credits before future utilization. In addition, as a result of the Azur Merger, until 2022 we were subject to certain limitations under the Internal Revenue Code in relation to the utilization of U.S. NOLs to offset U.S. taxable income resulting from certain transactions.

Valuation allowances require an assessment of both positive and negative evidence when determining whether it is more likely than not that deferred tax assets are recoverable. Such assessment is required by tax-paying component. Our valuation allowance was \$509.2 million and \$312.3 million as of December 31, 2024 and 2023, respectively, for certain Irish, U.S. (federal and state) and foreign deferred tax assets which we maintain until sufficient positive evidence exists to support reversal. As part of the overall change in valuation allowance, we recognized a net income tax expense of \$202.0 million, \$76.2 million and \$95.1 million in 2024, 2023 and 2022, respectively, relating primarily to the creation of a valuation allowance against certain deferred tax assets primarily associated with carryforwards in foreign subsidiaries and foreign tax credit carryforwards in Ireland. We periodically evaluate the likelihood of the realization of deferred tax assets and will adjust such amounts in light of changing facts and circumstances including, but not limited to, future projections of taxable income, tax legislation, rulings by relevant taxing authorities, the progress of tax examinations and the regulatory approval of products currently under development. Realization of the deferred tax assets is dependent on future taxable income. The Company believes that it is more likely than not to generate sufficient taxable income to realize the deferred tax assets carried as of December 31, 2024 for which no valuation allowance has been recognized.

No provision has been made for income tax on undistributed earnings of the Company's foreign subsidiaries where such earnings are considered indefinitely reinvested in the foreign operations. Temporary differences related to such earnings totaled \$1.6 billion as of December 31, 2024. In the event of the distribution of those earnings in the form of dividends, a sale of the subsidiaries, or certain other transactions, we may be liable for income taxes, subject to an adjustment, if any, for foreign tax credits. The Company estimates that it would incur additional income taxes of up to \$81.0 million on repatriation of these unremitted earnings to Ireland.

We only recognize the financial statement effects of a tax position when it is more likely than not, based on the technical merits, that the position will be sustained upon examination. As a result, we have recorded an unrecognized tax benefit for certain tax positions which we judge may not be sustained upon examination.

A reconciliation of our unrecognized tax benefits follows (in thousands):

	December 31,					
	2024		2023		2022	
Balance at the beginning of the year	\$	122,694	\$	143,976	\$	137,867
Increases related to current year tax positions		32,559		15,004		25,128
Increases related to prior year tax positions		—		224		2,794
Decreases related to prior year tax positions		(150)		(12,702)		(164)
Decreases related to settlements with taxing authorities		(2,605)		—		(223)
Lapse of the applicable statute of limitations		(26,520)		(23,808)		(21,426)
Balance at the end of the year	\$	125,978	\$	122,694	\$	143,976

The unrecognized tax benefits were included in income taxes payable, other non-current liabilities and deferred tax assets, net, in our consolidated balance sheets. Interest related to income taxes is recorded in income tax benefit in our consolidated statements of income (loss). As of December 31, 2024 and 2023, our accrued interest related to income taxes was \$8.6 million and \$8.4 million, respectively. Interest related to income taxes recognized in the consolidated statements of income (loss) were not significant. Included in the balance of unrecognized tax benefits were potential benefits of \$86.8 million and \$77.1 million at December 31, 2024 and 2023, respectively, that, if recognized, would affect the effective tax rate on income. The Company believes that it is reasonably possible that \$26.7 million of its currently remaining unrecognized tax benefits may be recognized by the end of 2025 as a result of a lapse of the statute of limitations.

We file income tax returns in multiple tax jurisdictions, the most significant of which are Ireland, the U.K. and the U.S. (both at the federal level and in various state jurisdictions). For Ireland we are no longer subject to income tax examinations by taxing authorities for the years prior to 2020. For the U.K. we are no longer subject to income tax examinations by taxing authorities for the years prior to 2016. The U.S. jurisdictions generally have statute of limitations three to four years from the later of the return due date or the date when the return was filed. However, in the U.S. (at the federal level and in most states), carryforwards that were generated in 2020 and earlier may still be adjusted upon examination by the taxing authorities. Certain of our Luxembourg subsidiaries are currently under examination by the Luxembourg taxing authorities for the years ended December 31, 2017, 2018 and 2019. In October 2022 and January 2023, we received tax assessment notices from the Luxembourg taxing authorities for all open tax years relating to certain transfer pricing and other adjustments. The notices propose additional Luxembourg income tax of approximately \$23.3 million, translated at the foreign exchange rate as at December 31, 2024. We disagree with the proposed assessments and are contesting them vigorously.

The Government of Ireland, the jurisdiction in which Jazz Pharmaceuticals Plc is incorporated, transposed the Global Minimum Tax Pillar Two rules into domestic legislation as part of the Finance (No. 2) Act 2023 (the "Finance Act"). The Finance Act closely follows the EU Minimum Tax Directive and certain OECD Guidance released to date. The Company is within the scope of these rules, which took effect from January 1, 2024. Under the new legislation, we are liable to pay a top-up tax for the difference between the Pillar Two effective tax rate per jurisdiction and the 15% minimum rate. The rules on how to calculate the Pillar Two effective tax rate are detailed and highly complex and specific adjustments envisaged in the Pillar Two legislation can give rise to different effective tax rates compared to those calculated for accounting purposes. We account for Pillar Two top-up taxes as a current tax when they are incurred. We do not believe we were subject to the top-up tax in 2024. The proportion of our profit before tax which is subject to the top-up tax and our exposure to Pillar Two top-up taxes in future years will depend on factors such as future revenues, costs and foreign currency exchange rates. We will continue to monitor changes in law and guidance in relation to Pillar Two.

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**Valuation and Qualifying Accounts
(In thousands)**

		Balance at beginning of period	Additions charged to costs and expenses	Other Additions	Deductions	Balance at end of period
For the year ended December 31, 2024						
Allowance for doubtful accounts	(1)	\$ 242	\$ 5,981	\$ —	\$ —	\$ 6,223
Allowance for sales discounts	(1)	5,962	24,334	—	(16,253)	14,043
Allowance for chargebacks	(1)	14,932	212,389	—	(214,896)	12,425
Deferred tax asset valuation allowance	(2)(3)	312,340	205,894	—	(9,044)	509,190
For the year ended December 31, 2023						
Allowance for doubtful accounts	(1)	\$ 242	\$ —	\$ —	\$ —	\$ 242
Allowance for sales discounts	(1)	2,980	22,334	—	(19,352)	5,962
Allowance for chargebacks	(1)	14,621	185,886	—	(185,575)	14,932
Deferred tax asset valuation allowance	(2)(3)	234,732	76,670	1,368	(430)	312,340
For the year ended December 31, 2022						
Allowance for doubtful accounts	(1)	\$ 298	\$ —	\$ —	\$ (56)	\$ 242
Allowance for sales discounts	(1)	2,126	20,133	—	(19,279)	2,980
Allowance for chargebacks	(1)	11,389	135,854	—	(132,622)	14,621
Deferred tax asset valuation allowance	(2)(3)	154,255	95,947	—	(15,470)	234,732

- (1) Shown as a reduction of accounts receivable. Charges related to sales discounts and chargebacks are reflected as a reduction of revenue.
- (2) Additions to the deferred tax asset valuation allowance charged to costs and expenses relate to movements on certain Irish, U.S. (federal and state) and other foreign deferred tax assets where we continue to maintain a valuation allowance until sufficient positive evidence exists to support reversal.
- (3) Deductions from the deferred tax asset valuation allowance include movements relating to utilization of NOLs and tax credit carryforwards, release in valuation allowance and other movements including adjustments following finalization of tax returns and currency translation adjustments.

EXHIBIT 19

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use LUMRYZ™ safely and effectively. See full prescribing information for LUMRYZ.

LUMRYZ (sodium oxybate) for extended-release oral suspension, CIII
Initial U.S. Approval: 2002

WARNING: CENTRAL NERVOUS SYSTEM (CNS) DEPRESSION AND ABUSE AND MISUSE

See full prescribing information for complete boxed warning.

Central Nervous System Depression

• LUMRYZ is a CNS depressant, and respiratory depression can occur with LUMRYZ use (5.1, 5.4)

Abuse and Misuse

• LUMRYZ is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB is associated with CNS adverse reactions, including seizure, respiratory depression, decreased consciousness, coma, and death (5.2, 9.2)

LUMRYZ is available only through a restricted program called the LUMRYZ REMS (5.3)

RECENT MAJOR CHANGES

Indications and Usage (1)	10/2024
Dosage and Administration (2.2)	10/2024
Warnings and Precautions (5.4, 5.5, 5.6, 5.7)	10/2024

INDICATIONS AND USAGE

LUMRYZ is a central nervous system depressant indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy (1).

DOSAGE AND ADMINISTRATION

Dosing for Adults:

- Initiate dosage at 4.5 g once per night orally (2.1).
- Titrate to effect in increments of 1.5 g per night at weekly intervals (2.1).
- Recommended dosage range: 6 g to 9 g once per night orally (2.1).

Dosing for Pediatric Patients (7 Years of Age and Older):

- The recommended starting dosage, titration regimen, and maximum total nightly dosage are based on body weight (2.2)
- **Pediatric patients 7 years and older weighing at least 45 kg:** The recommended starting dosage is 4.5 g once per night. Increase the dosage by 1.5 g per night at weekly intervals to the maximum recommended dosage of 9 g once per night orally. The dosage may be gradually titrated based on efficacy and tolerability (2.2).
- **Pediatric patients 7 years and older weighing less than 45 kg:** Because the recommended starting dosage cannot be achieved with the available strengths of LUMRYZ, use another sodium oxybate product to initiate treatment (2.2).

Important Administration Information

- Prepare the dose of LUMRYZ prior to bedtime; suspend dose in approximately ½ cup of water in the mixing cup provided (2.3).
- Allow 2 hours after eating before dosing (2.3).
- Take LUMRYZ while in bed and lie down after dosing (2.3).

DOSAGE FORMS AND STRENGTHS

For extended-release oral suspension: Packets of 4.5 g, 6 g, 7.5 g, or 9 g (3)

CONTRAINDICATIONS

- In combination with sedative hypnotics or alcohol (4).
- Succinic semialdehyde dehydrogenase deficiency (4).

WARNINGS AND PRECAUTIONS

- CNS depression: Use caution when considering the concurrent use of LUMRYZ with other CNS depressants (5.1).
- Caution patients against hazardous activities requiring complete mental alertness or motor coordination within the first 6 hours of dosing or after first initiating treatment until certain that LUMRYZ does not affect them adversely (5.1).
- Depression and suicidality: Monitor patients for emergent or increased depression and suicidality (5.5).
- Confusion/Anxiety: Monitor for impaired motor/cognitive function (5.6).
- Parasomnias: Evaluate episodes of sleepwalking (5.7).
- High sodium content in LUMRYZ: Monitor patients with heart failure, hypertension, or impaired renal function (5.8).

ADVERSE REACTIONS

Most common adverse reactions in adults (incidence ≥ 5% and greater than placebo) reported for any dose of LUMRYZ were nausea, dizziness, enuresis, headache, and vomiting (6.1).

Most common adverse reactions for pediatric patients (≥ 5%) in a study with immediate-release sodium oxybate were nausea, enuresis, vomiting, headache, weight decreased, decreased appetite, dizziness, and sleepwalking (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Avadel CNS Pharmaceuticals, LLC at 1-888-828-2335 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm (8.1).
- Geriatric patients: Monitor for impaired motor and/or cognitive function when taking LUMRYZ (8.5).
- Hepatic Impairment: Because of an increase in exposure, LUMRYZ should not be initiated in patients with hepatic impairment because appropriate dosage adjustments for initiation of LUMRYZ cannot be made (8.6).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

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17 PATIENT COUNSELING INFORMATION

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FULL PRESCRIBING INFORMATION

WARNING: CENTRAL NERVOUS SYSTEM (CNS) DEPRESSION AND ABUSE AND MISUSE

Central Nervous System Depression

LUMRYZ (sodium oxybate) is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with LUMRYZ at recommended doses [see *Warnings and Precautions (5.1)*]. Many patients who received sodium oxybate during clinical trials in narcolepsy were receiving central nervous system stimulants [see *Clinical Trials (14)*].

Abuse and Misuse

LUMRYZ (sodium oxybate) is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death [see *Warnings and Precautions (5.2)*].

Because of the risks of CNS depression and abuse and misuse, LUMRYZ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LUMRYZ REMS [see *Warnings and Precautions (5.3)*].

1 INDICATIONS AND USAGE

LUMRYZ is indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

2 DOSAGE AND ADMINISTRATION

2.1 Adult Dosing Information

The recommended starting dosage of LUMRYZ in adults is 4.5 grams (g) once per night administered orally. Increase the dosage by 1.5 g per night at weekly intervals to the recommended dosage range of 6 g to 9 g once per night orally. The dosage may be gradually titrated based on efficacy and tolerability. Doses higher than 9 g per night have not been studied and should not ordinarily be administered.

2.2 Pediatric Dosing Information

The recommended starting pediatric dosage, titration regimen, and maximum total nightly dosage are based on patient weight.

Pediatric Patients 7 years and Older Weighing at least 45 kg

The recommended starting dosage of LUMRYZ in pediatric patients 7 years and older weighing at least 45 kg is 4.5 g once per night administered orally. Increase the dosage by 1.5 g per night at weekly intervals to the maximum recommended dosage of 9 g once per night orally. The dosage may be gradually titrated based on efficacy and tolerability.

Pediatric Patients 7 years and Older Weighing Less than 45 kg

Because the recommended starting dosage in pediatric patients 7 years and older weighing less than 45 kg cannot be achieved with the available strengths of LUMRYZ, use another sodium oxybate product to initiate treatment. Refer to the Prescribing Information of other sodium oxybate products for the recommended dosage for those products.

The maximum recommended dosage for patients 7 years and older weighing 20 kg to <30 kg is 6 g once per night orally, and the maximum recommended dosage for patients 7 years and older weighing 30 kg to <45 kg is 7.5 g once per night orally [see *Dosage and Administration (2.4)*]. There is insufficient information to provide specific dosing recommendations for patients 7 years and older who weigh less than 20 kg.

2.3 Important Administration Instructions

LUMRYZ is taken orally as a single dose at bedtime. Prepare the dose of LUMRYZ prior to bedtime. Prior to ingestion, the dose of LUMRYZ should be suspended in approximately 1/3 cup (approximately 80 mL) of water in the mixing cup provided [see *Instructions for Use*]. Do not use hot water [see *Clinical Pharmacology (12.3)*]. After mixing, consume LUMRYZ within 30 minutes.

Take LUMRYZ at least 2 hours after eating [see *Clinical Pharmacology (12.3)*].

Patients should take LUMRYZ while in bed and lie down immediately after dosing as LUMRYZ may cause them to fall asleep abruptly without first feeling drowsy. Patients will often fall asleep within 5 minutes of taking LUMRYZ, and will usually fall asleep within 15 minutes, though the time it takes any individual patient to fall asleep may vary from night to night. Patients should remain in bed following ingestion of LUMRYZ.

2.4 Switching Patients from Immediate-Release Sodium Oxybate

Patients who are currently being treated with immediate-release sodium oxybate may be switched to LUMRYZ at the nearest equivalent dosage in grams per night (e.g., 7.5 g sodium oxybate divided into two 3.75 g doses per night to 7.5 g LUMRYZ once per night).

3 DOSAGE FORMS AND STRENGTHS

For extended-release oral suspension: LUMRYZ is a white to off-white powder provided in packets of 4.5 g, 6 g, 7.5 g, or 9 g of sodium oxybate.

4 CONTRAINDICATIONS

LUMRYZ is contraindicated for use in:

- combination with sedative hypnotics [see *Warnings and Precautions (5.1)*]

- combination with alcohol [*see Warnings and Precautions (5.1)*]
- patients with succinic semialdehyde dehydrogenase deficiency [*see Clinical Pharmacology (12.3)*]

5 WARNINGS AND PRECAUTIONS

5.1 Central Nervous System Depression

LUMRYZ is a central nervous system (CNS) depressant. Clinically significant respiratory depression and obtundation has occurred in patients treated with immediate-release sodium oxybate at recommended doses in clinical trials and may occur in patients treated with LUMRYZ at recommended doses. LUMRYZ is contraindicated in combination with alcohol and sedative hypnotics. The concurrent use of LUMRYZ with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating antiepileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death. If use of these CNS depressants in combination with LUMRYZ is required, dose reduction or discontinuation of one or more CNS depressants (including LUMRYZ) should be considered. In addition, if short-term use of an opioid (e.g., post- or perioperative) is required, interruption of treatment with LUMRYZ should be considered. In addition to coadministration of LUMRYZ and alcohol being contraindicated because of respiratory depression, consumption of alcohol while taking LUMRYZ may also result in a more rapid release of the dose of sodium oxybate [*see Clinical Pharmacology (12.3)*].

Healthcare providers should caution patients about operating hazardous machinery, including automobiles or airplanes, until they are reasonably certain that LUMRYZ does not affect them adversely (e.g., impair judgment, thinking, or motor skills). Patients should not engage in hazardous occupations or activities requiring complete mental alertness or motor coordination, such as operating machinery or a motor vehicle or flying an airplane, for at least 6 hours after taking LUMRYZ. Patients should be queried about CNS depression-related events upon initiation of LUMRYZ therapy and periodically thereafter.

LUMRYZ is available only through a restricted program under a REMS [*see Warnings and Precautions (5.3)*].

5.2 Abuse and Misuse

LUMRYZ is a Schedule III controlled substance. The active ingredient of LUMRYZ, sodium oxybate, is the sodium salt of gamma-hydroxybutyrate (GHB), a Schedule I controlled substance. Abuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. The rapid onset of sedation, coupled with the amnestic features of GHB, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g., assault victim). Because illicit use and abuse of GHB have been reported, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB

(e.g., increase in size or frequency of dosing, drug-seeking behavior, feigned cataplexy) [see *Warnings and Precautions (5.3) and Drug Abuse and Dependence (9.2)*].

LUMRYZ is available only through a restricted program under a REMS [see *Warnings and Precautions (5.3)*].

5.3 LUMRYZ REMS

LUMRYZ is available only through a restricted distribution program called the LUMRYZ REMS because of the risks of central nervous system depression and abuse and misuse [see *Warnings and Precautions (5.1, 5.2)*].

Notable requirements of the LUMRYZ REMS include the following:

- Healthcare providers who prescribe LUMRYZ are specially certified.
- LUMRYZ will be dispensed only by pharmacies that are specially certified.
- LUMRYZ will be dispensed and shipped only to patients who are enrolled in the LUMRYZ REMS with documentation of safe use conditions.

Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

5.4 Respiratory Depression and Sleep-Disordered Breathing

LUMRYZ may impair respiratory drive, especially in patients with compromised respiratory function. In overdoses of oxybate and with illicit use of GHB, life-threatening respiratory depression has been reported [see *Overdosage (10)*].

Increased apnea and reduced oxygenation may occur with LUMRYZ administration. A significant increase in the number of central apneas and clinically significant oxygen desaturation may occur in patients with obstructive sleep apnea treated with LUMRYZ.

During polysomnographic evaluation (PSG), central sleep apnea and oxygen desaturation were observed in pediatric patients with narcolepsy treated with immediate-release sodium oxybate.

In adult clinical trials of LUMRYZ in patients with narcolepsy, no subjects with apnea/hypopnea indexes greater than 15 were allowed to enroll.

In an adult study assessing the respiratory-depressant effects of immediate-release sodium oxybate at doses up to 9 g per night in 21 patients with narcolepsy, no dose-related changes in oxygen saturation were demonstrated in the group as a whole. One of four patients with preexisting moderate-to-severe sleep apnea had significant worsening of the apnea/hypopnea index during treatment.

In an adult study assessing the effects of immediate-release sodium oxybate 9 g per night in 50 patients with obstructive sleep apnea, immediate-release sodium oxybate did not increase the severity of sleep-disordered breathing and did not adversely affect the average duration and severity of oxygen desaturation overall. However, there was a significant increase in the number of central apneas in patients taking immediate-release sodium oxybate, and clinically significant oxygen desaturation ($\leq 55\%$) was measured in three patients (6%) after administration, with one patient withdrawing from the study and two continuing after single brief instances of desaturation.

In adult clinical trials in 128 patients with narcolepsy administered immediate-release sodium oxybate, two subjects had profound CNS depression, which resolved after supportive respiratory intervention. Two other patients discontinued immediate-release sodium oxybate because of severe difficulty breathing and an increase in obstructive sleep apnea. In two controlled trials assessing polysomnographic (PSG) measures in adult patients with narcolepsy administered immediate-release sodium oxybate, 40 of 477 patients were included with a baseline apnea/hypopnea index of 16 to 67 events per hour, indicative of mild to severe sleep-disordered breathing. None of the 40 patients had a clinically significant worsening of respiratory function, as measured by apnea/hypopnea index and pulse oximetry at doses of 4.5 g to 9 g per night.

Prescribers should be aware that sleep-related breathing disorders tend to be more prevalent in obese patients, in men, in postmenopausal women not on hormone replacement therapy, and among patients with narcolepsy. Increased central apneas and clinically relevant desaturation events have been observed with immediate-release sodium oxybate administration in adult and pediatric patients.

5.5 Depression and Suicidality

Depression, and suicidal ideation and behavior, can occur in patients treated with LUMRYZ.

In an adult clinical trial in patients with narcolepsy administered LUMRYZ [*see Adverse Reactions (6.1)*], there were no suicide attempts, but one patient developed suicidal ideation at the 9 g dose. In adult clinical trials in patients with narcolepsy (n=781) administered immediate-release sodium oxybate, there were two suicides and two attempted suicides in patients treated with immediate-release sodium oxybate, including three patients with a previous history of depressive psychiatric disorder. Of the two suicides, one patient used immediate-release sodium oxybate in conjunction with other drugs. Immediate-release sodium oxybate was not involved in the second suicide. Adverse reactions of depression were reported by 7% of 781 patients treated with immediate-release sodium oxybate, with four patients (<1%) discontinuing because of depression. In most cases, no change in immediate-release sodium oxybate treatment was required.

In a controlled trial in adults with narcolepsy administered LUMRYZ where patients were titrated from 4.5 g to 9 g per night, the incidences of depression were 0% at 4.5 g, 1% at 6 g, 1.1% at 7.5 g, and 1.3% at 9 g. In a controlled adult trial, with patients randomized to fixed doses of 3 g, 6 g, or 9 g per night immediate-release sodium oxybate or placebo, there was a single event of depression at the 3 g per night dose. In another adult controlled trial, with patients titrated from an initial 4.5 g per night starting dose of immediate-release sodium oxybate, the incidences of depression were 1.7%, 1.5%, 3.2%, and 3.6% for the placebo, 4.5 g, 6 g, and 9 g per night doses, respectively.

In a clinical trial in pediatric patients with narcolepsy (n=104) administered immediate-release sodium oxybate, one patient experienced suicidal ideation and two patients reported depression while taking immediate-release sodium oxybate.

The emergence of depression in patients treated with LUMRYZ requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking LUMRYZ.

5.6 Other Behavioral or Psychiatric Adverse Reactions

Other behavioral and psychiatric adverse reactions can occur in patients taking LUMRYZ.

During adult clinical trials in patients with narcolepsy administered LUMRYZ, 2% of 107 patients treated with LUMRYZ experienced a confusional state. During adult clinical trials in patients with narcolepsy administered immediate-release sodium oxybate, 3% of 781 patients treated with immediate-release sodium oxybate experienced confusion, with incidence generally increasing with dose.

No patients treated with LUMRYZ discontinued treatment because of confusion. Less than 1% of patients discontinued the immediate-release sodium oxybate because of confusion. Confusion was reported at all recommended doses of immediate-release sodium oxybate from 6 g to 9 g per night. In a controlled trial in adults where patients were randomized to immediate-release sodium oxybate in fixed total daily doses of 3 g, 6 g, or 9 g per night or placebo, a dose-response relationship for confusion was demonstrated, with 17% of patients at 9 g per night experiencing confusion. In that controlled trial, the confusion resolved in all cases soon after termination of treatment. In one trial where immediate-release sodium oxybate was titrated from an initial 4.5 g per night dose, there was a single event of confusion in one patient at the 9 g per night dose. In the majority of cases in all adult clinical trials in patients with narcolepsy administered immediate-release sodium oxybate, confusion resolved either soon after termination of dosing or with continued treatment.

Anxiety occurred in 7.5% of 107 patients treated with LUMRYZ in the adult trial in patients with narcolepsy. Anxiety occurred in 5.8% of the 874 patients receiving immediate-release sodium oxybate in adult clinical trials in another population.

Other psychiatric reactions reported in adult clinical trials in patients with narcolepsy administered LUMRYZ included irritability, emotional disorder, panic attack, agitation, delirium, and obsessive thoughts. Other neuropsychiatric reactions reported in adult clinical trials in patients with narcolepsy administered immediate-release sodium oxybate and in the postmarketing setting for immediate-release sodium oxybate include hallucinations, paranoia, psychosis, aggression, and agitation.

In a clinical trial in pediatric patients with narcolepsy administered immediate-release sodium oxybate, neuropsychiatric reactions, including acute psychosis, confusion, and anxiety were reported while taking immediate-release sodium oxybate.

The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking LUMRYZ should be carefully monitored.

5.7 Parasomnias

Parasomnias can occur in patients taking LUMRYZ.

Sleepwalking, defined as confused behavior occurring at night and at times associated with wandering, was reported in 3% of 107 adult patients with narcolepsy treated with LUMRYZ. No patients treated with LUMRYZ discontinued due to sleepwalking. Sleepwalking was reported in 6% of 781 patients with narcolepsy treated with immediate-release sodium oxybate in adult controlled and long-term open-label studies, with <1% of patients discontinuing due to sleepwalking. In controlled trials, rates of sleepwalking were similar for patients taking placebo

and patients taking immediate-release sodium oxybate. It is unclear if some or all of the reported sleepwalking episodes correspond to true somnambulism, which is a parasomnia occurring during non-REM sleep, or to any other specific medical disorder. Five instances of sleepwalking with potential injury or significant injury were reported during a clinical trial of immediate-release sodium oxybate in patients with narcolepsy.

Parasomnias, including sleepwalking, have been reported in a pediatric clinical trial and in postmarketing experience with immediate-release sodium oxybate. Therefore, episodes of sleepwalking should be fully evaluated, and appropriate interventions considered.

5.8 Use in Patients Sensitive to High Sodium Intake

LUMRYZ has a high sodium content. In patients sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment), consider the amount of daily sodium intake in each dose of LUMRYZ. Table 1 provides the approximate sodium content per LUMRYZ dose.

Table 1: Approximate Sodium Content per Total Nightly Dose of LUMRYZ (g = grams)

LUMRYZ Dose	Sodium Content/Total Nightly Exposure
4.5 g per night	820 mg
6 g per night	1100 mg
7.5 g per night	1400 mg
9 g per night	1640 mg

6 ADVERSE REACTIONS

The following clinically significant adverse reactions appear in other sections of the labeling:

- CNS Depression *[see Warnings and Precautions (5.1)]*
- Abuse and Misuse *[see Warnings and Precautions (5.2)]*
- Respiratory Depression and Sleep-Disordered Breathing *[see Warnings and Precautions (5.4)]*
- Depression and Suicidality *[see Warnings and Precautions (5.5)]*
- Other Behavioral or Psychiatric Adverse Reactions *[see Warnings and Precautions (5.6)]*
- Parasomnias *[see Warnings and Precautions (5.7)]*
- Use in Patients Sensitive to High Sodium Intake *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Adult Patients

LUMRYZ was studied in one placebo-controlled trial (Study 1) [see *Clinical Studies (14.1)*] in 212 patients with narcolepsy (107 patients treated with LUMRYZ and 105 with placebo).

Adverse Reactions Leading to Treatment Discontinuation

In Study 1, 15.9% of patients treated with LUMRYZ discontinued because of adverse reactions, compared to 1.9% of patients receiving placebo. The most common adverse reaction leading to discontinuation was dizziness (4.7%). For LUMRYZ, 5.6% of patients discontinued due to adverse reactions on 4.5 g, 4.1% on 6 g, 4.5% on 7.5 g, and 3.9% on 9 g dose.

Most Common Adverse Reactions

The most common adverse reactions (incidence $\geq 5\%$ and greater than placebo) reported for any dose of LUMRYZ were nausea, dizziness, enuresis, headache, and vomiting.

Adverse Reactions Occurring at an Incidence of 2% or Greater

Table 2 lists adverse reactions occurring in 2% or more of LUMRYZ-treated patients on any individual dose and at a rate greater than placebo-treated patients in Study 1.

Table 2: Adverse Reactions Occurring in 2% or More of LUMRYZ-Treated Adult Patients and Greater than for Placebo-Treated Patients in Study 1

Adverse Reaction	Placebo (N=105) %	LUMRYZ 4.5 g (N=107) %	LUMRYZ 6 g (N=97) %	LUMRYZ 7.5 g (N=88) %	LUMRYZ 9 g (N=77) %
Gastrointestinal Disorders					
Vomiting	2	3	3	6	5
Nausea	3	6	8	7	1
Investigations					
Weight Decreased	0	1	0	0	4
Metabolism and Nutritional Disorders					
Decreased Appetite	0	4	4	3	3
Nervous System Disorders					
Dizziness	0	6	4	6	5
Somnolence	1	0	1	2	4
Headache	6	7	5	6	0
Psychiatric Disorders					
Enuresis	0	2	4	9	9
Anxiety	1	3	1	3	1
Somnambulism	0	1	2	0	0

Dose-Response Information

In the clinical trial in adult patients with narcolepsy, a dose-response relationship was observed for enuresis and somnolence.

Additional Adverse Reactions

Adverse reactions observed in clinical studies with immediate-release sodium oxybate ($\geq 2\%$), but not observed in Study 1 at a frequency of higher than 2%, and which may be relevant for LUMRYZ: diarrhea, abdominal pain upper, dry mouth, pain, feeling drunk, peripheral edema, cataplexy, muscle spasms, pain in extremity, tremor, disturbance in attention, paresthesia, sleep paralysis, disorientation, irritability, and hyperhidrosis.

Pediatric Patients (7 Years of Age and Older)

The safety of LUMRYZ for the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy is supported by an adequate and well-controlled trial of immediate-release sodium oxybate [see *Clinical Studies (14.2)*]. Below is a display of adverse reactions of immediate-release sodium oxybate in this adequate and well-controlled trial.

In this trial, 104 patients aged 7 to 17 years (37 patients aged 7 to 11 years; 67 patients aged 12 to 17 years) with narcolepsy received immediate-release sodium oxybate for up to one year. This trial included an open-label safety continuation period in which eligible patients received immediate-release sodium oxybate for up to an additional 2 years. The median and maximum exposure across the entire trial were 371 and 987 days, respectively.

Adverse Reactions Leading to Treatment Discontinuation

In the pediatric clinical trial with immediate-release sodium oxybate, 7 of 104 patients reported adverse reactions that led to withdrawal from the study (hallucination, tactile; suicidal ideation; weight decreased; sleep apnea syndrome; affect lability; anger, anxiety, depression; and headache).

Adverse Reactions in the Pediatric Clinical Trial

The most common adverse reactions ($\geq 5\%$) were nausea (20%), enuresis (19%), vomiting (18%), headache (17%), weight decreased (13%), decreased appetite (9%), dizziness (8%), and sleepwalking (6%).

Additional information regarding safety in pediatric patients appears in the following sections:

- Respiratory Depression and Sleep-Disordered Breathing [see *Warnings and Precautions (5.4)*]
- Depression and Suicidality [see *Warnings and Precautions (5.5)*]
- Other Behavioral or Psychiatric Adverse Reactions [see *Warnings and Precautions (5.6)*]
- Parasomnias [see *Warnings and Precautions (5.7)*]

The overall adverse reaction profile of immediate-release sodium oxybate in the pediatric clinical trial was similar to that seen in the adult clinical trial with immediate-release sodium oxybate. The safety profile in pediatric patients with LUMRYZ is expected to be similar to that of adult patients treated with LUMRYZ and to that of pediatric patients treated with immediate-release sodium oxybate.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of sodium oxybate. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure:

Arthralgia, decreased appetite, fall*, fluid retention, hangover, headache, hypersensitivity, hypertension, memory impairment, nocturia, panic attack, vision blurred, and weight decreased.

*The sudden onset of sleep in patients taking sodium oxybate, including in a standing position or while rising from bed, has led to falls complicated by injuries, in some cases requiring hospitalization.

7 DRUG INTERACTIONS

7.1 Alcohol, Sedative Hypnotics, and CNS Depressants

LUMRYZ is contraindicated for use in combination with alcohol or sedative hypnotics. Use of other CNS depressants may potentiate the CNS-depressant effects of LUMRYZ [see *Warnings and Precautions* (5.1)]. In addition to coadministration of LUMRYZ and alcohol being contraindicated because of respiratory depression, consumption of alcohol while taking LUMRYZ may also result in a more rapid release of the dose of sodium oxybate [see *Clinical Pharmacology* (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of sodium oxybate in pregnant women. Oral administration of sodium oxybate to pregnant rats (150, 350, or 1,000 mg/kg/day) or rabbits (300, 600, or 1,200 mg/kg/day) throughout organogenesis produced no clear evidence of developmental toxicity; however, oral administration to rats throughout pregnancy and lactation resulted in increased stillbirths and decreased offspring postnatal viability and growth, at a clinically relevant dose [see *Data*].

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Clinical Considerations

Labor or Delivery

LUMRYZ has not been studied in labor or delivery. In obstetric anesthesia using an injectable formulation of sodium oxybate, newborns had stable cardiovascular and respiratory measures but were very sleepy, causing a slight decrease in Apgar scores. There was a fall in the rate of uterine

contractions 20 minutes after injection. Placental transfer is rapid and gamma-hydroxybutyrate (GHB) has been detected in newborns at delivery after intravenous administration of GHB to mothers. Subsequent effects of sodium oxybate on later growth, development, and maturation in humans are unknown.

Data

Animal Data

Oral administration of sodium oxybate to pregnant rats (150, 350, or 1,000 mg/kg/day) or rabbits (300, 600, or 1,200 mg/kg/day) throughout organogenesis produced no clear evidence of developmental toxicity. The highest doses tested in rats and rabbits were approximately 1 and 3 times, respectively, the maximum recommended human dose (MRHD) of 9 g per night on a body surface area (mg/m²) basis.

Oral administration of sodium oxybate (150, 350, or 1,000 mg/kg/day) to rats throughout pregnancy and lactation resulted in increased stillbirths and decreased offspring postnatal viability and body weight gain at the highest dose tested. The no-effect dose for pre- and postnatal developmental toxicity in rats is less than the MRHD on a mg/m² basis.

8.2 Lactation

Risk Summary

GHB is excreted in human milk after oral administration of sodium oxybate. There is insufficient information on the risk to a breastfed infant, and there is insufficient information on milk production in nursing mothers. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for LUMRYZ and any potential adverse effects on the breastfed infant from LUMRYZ or from the underlying maternal condition.

8.4 Pediatric Use

LUMRYZ has not been studied in a pediatric clinical trial. The safety and effectiveness of LUMRYZ in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy is supported by evidence from a double-blind, placebo-controlled, randomized-withdrawal study of immediate-release sodium oxybate [see *Adverse Reactions* (6.1) and *Clinical Studies* (14.2)].

In the pediatric clinical trial with immediate-release sodium oxybate administration in pediatric patients 7 years of age and older with narcolepsy, serious adverse reactions of central sleep apnea and oxygen desaturation documented by polysomnography evaluation; depression; suicidal ideation; neuropsychiatric reactions including acute psychosis, confusion, and anxiety; and parasomnias, including sleepwalking, have been reported [see *Warnings and Precautions* (5.4, 5.5, 5.6, 5.7) and *Adverse Reactions* (6.1)].

The safety and effectiveness of LUMRYZ have not been established in pediatric patients younger than 7 years old.

Juvenile Animal Toxicity Data

In a study in which sodium oxybate (0, 100, 300, or 900 mg/kg/day) was orally administered to rats during the juvenile period of development (postnatal days 21 through 90), mortality was

observed at the two highest doses tested. Deaths occurred during the first week of dosing and were associated with clinical signs (including decreased activity and respiratory rate) consistent with the pharmacological effects of the drug. Reduced body weight gain in males and females and delayed sexual maturation in males were observed at the highest dose tested. The no-effect dose for adverse effects in juvenile rats is associated with plasma exposures (AUC) less than that at the maximum recommended human dose (9 g/night).

8.5 Geriatric Use

Clinical studies of LUMRYZ or immediate-release sodium oxybate in patients with narcolepsy did not include sufficient numbers of subjects age 65 years and older to determine whether they respond differently from younger subjects. In controlled trials of immediate-release sodium oxybate in another population, 39 (5%) of 874 patients were 65 years or older. Discontinuations of treatment due to adverse reactions were increased in the elderly compared to younger adults (21% vs. 19%). Frequency of headaches was markedly increased in the elderly (39% vs. 19%). The most common adverse reactions were similar in both age categories. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Hepatic Impairment

Because of an increase in exposure to LUMRYZ, LUMRYZ should not be initiated in patients with hepatic impairment because appropriate dosage adjustments for initiation of LUMRYZ cannot be made with the available dosage strengths [*see Clinical Pharmacology (12.3)*]. Patients with hepatic impairment who have been titrated to a maintenance dosage of another oxybate product can be switched to LUMRYZ if the appropriate dosage strength is available.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

LUMRYZ is a Schedule III controlled substance under the Federal Controlled Substances Act. Non-medical use of LUMRYZ could lead to penalties assessed under the higher Schedule I controls.

9.2 Abuse

LUMRYZ (sodium oxybate), the sodium salt of GHB, produces dose-dependent central nervous system effects, including hypnotic and positive subjective reinforcing effects. The onset of effect is rapid, enhancing its potential for abuse or misuse.

Drug abuse is the intentional non-therapeutic use of a drug product or substance, even once, for its desirable psychological or physiological effects. Misuse is the intentional use, for therapeutic purposes of a drug by an individual in a way other than prescribed by a healthcare provider or for whom it was not prescribed. Drug misuse and abuse may occur with or without progression to addiction. Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing

drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

The rapid onset of sedation, coupled with the amnestic features of GHB, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (e.g., assault victim).

Illicit GHB is abused in social settings primarily by young adults. Some of the doses estimated to be abused are in a similar dosage range to that used for treatment of patients with cataplexy. GHB has some commonalities with ethanol over a limited dose range, and some cross tolerance with ethanol has been reported as well. Cases of severe dependence and craving for GHB have been reported when the drug is taken around the clock. Patterns of abuse indicative of dependence include: 1) the use of increasingly large doses, 2) increased frequency of use, and 3) continued use despite adverse consequences.

Because illicit use and abuse of GHB have been reported, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB (e.g., increase in size or frequency of dosing, drug-seeking behavior, feigned cataplexy). Dispose of LUMRYZ according to state and federal regulations. It is safe to dispose of LUMRYZ down the sanitary sewer.

9.3 Dependence

Dependence

Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug. There have been case reports of withdrawal, ranging from mild to severe, following discontinuation of illicit use of GHB at frequent repeated doses (18 g to 250 g per day) in excess of the recommended dosage range. Signs and symptoms of GHB withdrawal following abrupt discontinuation included insomnia, restlessness, anxiety, psychosis, lethargy, nausea, tremor, sweating, muscle cramps, tachycardia, headache, dizziness, rebound fatigue and sleepiness, confusion, and, particularly in the case of severe withdrawal, visual hallucinations, agitation, and delirium. These symptoms generally abated in 3 to 14 days. In cases of severe withdrawal, hospitalization may be required. The discontinuation effects of LUMRYZ have not been systematically evaluated in controlled clinical trials. In the clinical trial experience with immediate-release sodium oxybate in narcolepsy/cataplexy patients at recommended doses, two patients reported anxiety and one reported insomnia following abrupt discontinuation at the termination of the clinical trial; in the two patients with anxiety, the frequency of cataplexy had increased markedly at the same time.

Tolerance

Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose). Tolerance to LUMRYZ has not been systematically studied in controlled clinical trials. There have been some case reports of symptoms of tolerance developing after illicit use at dosages far in excess of the recommended LUMRYZ dosage regimen. Clinical studies of immediate-release sodium oxybate in the treatment of alcohol

withdrawal suggest a potential cross-tolerance with alcohol. The safety and effectiveness of LUMRYZ in the treatment of alcohol withdrawal have not been established.

10 OVERDOSAGE

10.1 Human Experience

Information regarding overdose with LUMRYZ is derived largely from reports in the medical literature that describe symptoms and signs in individuals who have ingested GHB illicitly. In these circumstances, the co-ingestion of other drugs and alcohol was common and may have influenced the presentation and severity of clinical manifestations of overdose.

In adult clinical trials of immediate-release sodium oxybate, two cases of overdose with sodium oxybate were reported. In the first case, an estimated dose of 150 g, more than 15 times the maximum recommended dose, caused a patient to be unresponsive with brief periods of apnea and to be incontinent of urine and feces. This individual recovered without sequelae. In the second case, death was reported following a multiple drug overdose consisting of sodium oxybate and numerous other drugs.

10.2 Signs and Symptoms

Information about signs and symptoms associated with overdosage with LUMRYZ derives from reports of illicit use of GHB. Patient presentation following overdose is influenced by the dose ingested, the time since ingestion, the co-ingestion of other drugs and alcohol, and the fed or fasted state. Patients have exhibited varying degrees of depressed consciousness that may fluctuate rapidly between a confusional, agitated combative state with ataxia and coma. Emesis (even when obtunded), diaphoresis, headache, and impaired psychomotor skills have been observed. No typical pupillary changes have been described to assist in diagnosis; pupillary reactivity to light is maintained. Blurred vision has been reported. An increasing depth of coma and acidosis have been observed at higher doses. Myoclonus and tonic-clonic seizures have been reported.

Respiration may be unaffected or compromised in rate and depth. Cheyne-Stokes respiration and apnea have been observed. Bradycardia and hypothermia may accompany unconsciousness, as well as muscular hypotonia, but tendon reflexes remain intact.

10.3 Recommended Treatment of Overdose

General symptomatic and supportive care should be instituted immediately, and gastric decontamination may be considered if co-ingestants are suspected. Because emesis may occur in the presence of obtundation, appropriate posture (left lateral recumbent position) and protection of the airway by intubation may be warranted. Although the gag reflex may be absent in deeply comatose patients, even unconscious patients may become combative to intubation, and rapid-sequence induction (without the use of sedative) should be considered. Vital signs and consciousness should be closely monitored. The bradycardia reported with GHB overdose has been responsive to atropine intravenous administration. No reversal of the central depressant effects of LUMRYZ can be expected from naloxone or flumazenil administration. The use of hemodialysis and other forms of extracorporeal drug removal have not been studied in GHB

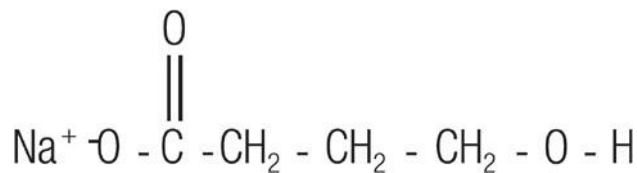
overdose, but have been reported in cases of acidosis associated with GHB ingestions of 125 g or greater; however, due to the rapid metabolism of sodium oxybate, these measures may not be warranted.

10.4 Poison Control Center

As with the management of all cases of drug overdosage, the possibility of multiple drug ingestion should be considered. The healthcare provider is encouraged to collect urine and blood samples for routine toxicologic screening, and to consult with a regional poison control center (1-800-222-1222) for current treatment recommendations.

11 DESCRIPTION

Sodium oxybate, a CNS depressant, is the active ingredient in LUMRYZ for extended-release oral suspension. The chemical name for sodium oxybate is sodium 4-hydroxybutyrate. The molecular formula is $C_4H_7NaO_3$, and the molecular weight is 126.09 g/mole. The chemical structure is:



Sodium oxybate is a white to off-white solid powder.

Each packet of LUMRYZ contains 4.5 g, 6 g, 7.5 g, or 9 g of sodium oxybate, equivalent to 3.7 g, 5.0 g, 6.2 g, or 7.4 g of oxybate, respectively. The inactive ingredients are carrageenan, hydrogenated vegetable oil, hydroxyethyl cellulose, magnesium stearate, malic acid, methacrylic acid copolymer, microcrystalline cellulose, povidone, and xanthan gum.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

LUMRYZ is a CNS depressant. The mechanism of action of LUMRYZ in the treatment of narcolepsy is unknown. Sodium oxybate is the sodium salt of gamma-hydroxybutyrate (GHB), an endogenous compound and metabolite of the neurotransmitter GABA. It is hypothesized that the therapeutic effects of LUMRYZ on cataplexy and excessive daytime sleepiness are mediated through GABA_B actions at noradrenergic and dopaminergic neurons, as well as at thalamocortical neurons.

12.3 Pharmacokinetics

Following oral administration of LUMRYZ, the plasma levels of GHB increased dose-proportionally for C_{max} and more than dose-proportionally for area under the plasma

concentration-time curve (AUC_{inf}) (respectively, 2-fold and 2.3-fold increases as total daily dose is doubled from 4.5 g to 9 g).

No clinically significant difference in oxybate pharmacokinetics was observed between a single 6 g dose of LUMRYZ and two 3 g doses of immediate-release sodium oxybate administered 4 hours apart.

Absorption

Following oral administration of a single 6 g dose of LUMRYZ, the peak plasma concentration (C_{max}) was 66 mcg/mL and the time to peak plasma concentration (T_{max}) was 1.5 hours.

Effect of Food

Administration of LUMRYZ immediately after a high-fat meal resulted in a mean reduction in C_{max} and AUC of GHB by 33% and 14%, respectively; average T_{max} increased from 0.5 hours to 1.5 hours [see *Dosage and Administration* (2.3)].

Effect of Ethanol

An in vitro study showed alcohol-induced dose-dumping of sodium oxybate from extended-release oral suspension at 1 hour in the presence of 40% alcohol, and approximately 60% increase of drug release at 2 hours in the presence of 20% alcohol [see *Contraindications* (4) and *Warnings and Precautions* (5.1)].

Effect of Water Temperature

An in vitro dissolution study showed that LUMRYZ mixed with hot water (90°C) resulted in a dose-dumping phenomenon for the release of sodium oxybate, whereas warm water (50°C) did not significantly affect the drug release from the extended-release suspension [see *Dosage and Administration* (2.3)].

Distribution

GHB is a hydrophilic compound with an apparent volume of distribution averaging 190 mL/kg to 384 mL/kg. At GHB concentrations ranging from 3 mcg/mL to 300 mcg/mL, less than 1% is bound to plasma proteins.

Elimination

Metabolism

Animal studies indicate that metabolism is the major elimination pathway for GHB, producing carbon dioxide and water via the tricarboxylic acid (Krebs) cycle, and secondarily by β -oxidation. The primary pathway involves a cytosolic NADP⁺-linked enzyme, GHB dehydrogenase, which catalyzes the conversion of GHB to succinic semialdehyde, which is then biotransformed to succinic acid by the enzyme succinic semialdehyde dehydrogenase. Succinic acid enters the Krebs cycle where it is metabolized to carbon dioxide and water. A second mitochondrial oxidoreductase enzyme, a transhydrogenase, also catalyzes the conversion to succinic semialdehyde in the presence of α -ketoglutarate. An alternate pathway of biotransformation involves β -oxidation via 3,4-dihydroxybutyrate to carbon dioxide and water. No active metabolites have been identified.

Excretion

The clearance of GHB is almost entirely by biotransformation to carbon dioxide, which is then eliminated by expiration. On average, less than 5% of unchanged drug appears in human urine within 6 to 8 hours after dosing. Fecal excretion is negligible. GHB has an elimination half-life of 0.5 to 1 hour.

Specific Population

Geriatric Patients

There is limited experience with LUMRYZ in the elderly. Results from a pharmacokinetic study of immediate-release sodium oxybate (n=20) in another studied population indicate that the pharmacokinetic characteristics of GHB are consistent among younger (age 48 to 64 years) and older (age 65 to 75 years) adults.

Pediatric Patients

The pharmacokinetics of LUMRYZ has not been directly evaluated in pediatric patients.

The pharmacokinetics of immediate-release sodium oxybate were evaluated in pediatric patients 7 to 17 years of age (n=29). The pharmacokinetic characteristics of immediate-release sodium oxybate were shown to be similar in adults and pediatric patients. Body weight was found to be the major intrinsic factor affecting oxybate pharmacokinetics.

Male and Female Patients

In a study of 18 female and 18 male healthy adult volunteers, no gender differences were detected in the pharmacokinetics of GHB following an immediate-release 4.5 g oral dose of sodium oxybate.

Racial or Ethnic Groups

There are insufficient data to evaluate any pharmacokinetic differences among races.

Patients with Renal Impairment

No pharmacokinetic study in patients with renal impairment has been conducted.

Patients with Hepatic Impairment

The pharmacokinetics of GHB in 16 cirrhotic patients, half without ascites (Child's Class A) and half with ascites (Child's Class C), were compared to the kinetics in 8 subjects with normal hepatic function, after a single sodium oxybate oral dose of 25 mg/kg. AUC values were doubled in cirrhotic patients, with apparent oral clearance reduced from 9.1 mL/min/kg in healthy adults to 4.5 and 4.1 mL/min/kg in Class A and Class C patients, respectively. Elimination half-life was significantly longer in Class C and Class A patients than in control patients (mean $t_{1/2}$ of 59 minutes and 32 minutes, respectively, versus 22 minutes in control patients). LUMRYZ should not be initiated in patients with liver impairment [see *Use in Specific Populations* (8.6)].

Drug Interaction Studies

In vitro studies with pooled human liver microsomes indicate that sodium oxybate does not significantly inhibit the activities of the human isoenzymes CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A, up to the concentration of 3 mM (378 mcg/mL), a level considerably higher than levels achieved with the maximum recommended dose.

A drug interaction study in healthy adults (age 18 to 55 years) was conducted with LUMRYZ and divalproex sodium. Co-administration of a single dose of LUMRYZ (6 g) with divalproex sodium ER at steady state resulted in an approximate 18% increase in AUC (90% CI ratio range of 112%-123%), which is not expected to be clinically meaningful, while C_{max} was comparable. A single dose of LUMRYZ (6 g) did not appear to affect the pharmacokinetics of divalproex sodium. However, a pharmacodynamic interaction between LUMRYZ and divalproex sodium, a sedative antiepileptic drug, cannot be ruled out [see *Warnings and Precautions (5.1) and Drug Interactions (7.1)*].

Drug interaction studies in healthy adults (age 18 to 50 years) were conducted with immediate-release sodium oxybate and diclofenac and ibuprofen:

- Diclofenac: Co-administration of sodium oxybate (6 g per day as two equal doses of 3 grams dosed four hours apart) with diclofenac (50 mg/dose twice per day) showed no significant changes in systemic exposure to GHB. Co-administration did not appear to affect the pharmacokinetics of diclofenac.
- Ibuprofen: Co-administration of sodium oxybate (6 g per day as two equal doses of 3 grams dosed four hours apart) with ibuprofen (800 mg/dose four times per day also dosed four hours apart) resulted in comparable systemic exposure to GHB, as shown by plasma C_{max} and AUC values. Co-administration did not affect the pharmacokinetics of ibuprofen.

Drug interaction studies in healthy adults demonstrated no pharmacokinetic interactions between immediate-release sodium oxybate and protriptyline hydrochloride, zolpidem tartrate, and modafinil. Also, there were no pharmacokinetic interactions with the alcohol dehydrogenase inhibitor fomepizole. However, pharmacodynamic interactions with these drugs cannot be ruled out. Alteration of gastric pH with omeprazole produced no significant change in the pharmacokinetics of GHB. In addition, drug interaction studies in healthy adults demonstrated no pharmacokinetic or clinically significant pharmacodynamic interactions between immediate-release sodium oxybate and duloxetine HCl.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Administration of sodium oxybate to rats at oral doses of up to 1,000 mg/kg/day for 83 (males) or 104 (females) weeks resulted in no increase in tumors. Plasma exposure (AUC) at the highest dose tested was 2 times that in humans at the maximum recommended human dose (MRHD) of 9 g per night.

The results of 2-year carcinogenicity studies in mouse and rat with gamma-butyrolactone, a compound that is metabolized to sodium oxybate *in vivo*, showed no clear evidence of carcinogenic activity. The plasma AUCs of sodium oxybate achieved at the highest doses tested in these studies were less than that in humans at the MRHD.

Mutagenesis

Sodium oxybate was negative in the *in vitro* bacterial gene mutation assay, an *in vitro* chromosomal aberration assay in mammalian cells, and in an *in vivo* rat micronucleus assay.

Impairment of Fertility

Oral administration of sodium oxybate (150, 350, or 1,000 mg/kg/day) to male and female rats prior to and throughout mating and continuing in females through early gestation resulted in no adverse effects on fertility. The highest dose tested is approximately equal to the MRHD on a mg/m² basis.

14 CLINICAL STUDIES

14.1 Cataplexy and Excessive Daytime Sleepiness (EDS) in Adult Narcolepsy

The effectiveness of LUMRYZ for the treatment of cataplexy or excessive daytime sleepiness (EDS) in adults with narcolepsy has been established based on a double-blind, randomized, placebo-controlled, two-arm multi-center study to assess the efficacy and safety of a once nightly administration of LUMRYZ in patients with narcolepsy (Study 1; NCT02720744).

A total of 212 patients were randomized to receive LUMRYZ or placebo in a 1:1 ratio and received at least one dose of study drug. The study was divided into four sequential study periods, and incorporated dose titration to stabilized dose administration of LUMRYZ (4.5 g, 6 g, 7.5 g, and 9 g). There was a three-week screening period, a 13-week treatment period including up-titration over a period of eight weeks, five weeks of stable dosing at 9 g/night, and a one-week follow-up period. Patients could be on concomitant stimulant as long as dosage was stable for 3 weeks prior to study start.

The three co-primary endpoints were the Maintenance of Wakefulness Test (MWT), Clinical Global Impression-Improvement (CGI-I), and mean change in weekly cataplexy attacks. The MWT measures latency to sleep onset (in minutes), averaged over five sessions at 2-hour intervals following nocturnal polysomnography. For each test session, patients were instructed to remain awake for as long as possible during 30-minute test sessions, and sleep latency was determined as the number of minutes patients could remain awake. The overall score was the mean sleep latency for the 5 sessions. The CGI-I was evaluated on a 7-point scale, centered at *No Change*, and ranging from *Very Much Worse* to *Very Much Improved*. Patients were rated by evaluators who based their assessments on the severity of narcolepsy at Baseline.

Demographic and mean baseline characteristics were similar for the LUMRYZ and placebo groups. A total of 76% were narcolepsy type 1 (NT1; with both symptoms of EDS and cataplexy) patients, and 24% were narcolepsy type 2 (NT2; with symptoms of EDS and without cataplexy) patients. The mean age was 31 years, and 68% were female. Approximately 63% of patients were on concomitant stimulant use. The mean MWT at baseline was 5 minutes for the LUMRYZ group, and 4.7 minutes for the placebo group. The mean number of cataplexy attacks per week at baseline was 18.9 in the LUMRYZ group and 19.8 in the placebo group. A statistically significant improvement was seen on the MWT, CGI-I, and mean weekly cataplexy attacks, for the 6 g (Week 3), 7.5 g (Week 8), and 9 g (Week 13) dose of LUMRYZ, compared to the placebo group (see Table 3, Table 4, and Table 5).

Table 3: Change from Baseline in the Maintenance of Wakefulness Test

Dose	Treatment Group (N)	Change from Baseline (Minutes)*	Difference from Placebo [95% CI]	p-value
6 g (Week 3)	LUMRYZ (87)	8.1	5.0 [2.90;7.05]	<0.001
	Placebo (88)	3.1	-	-
7.5 g (Week 8)	LUMRYZ (76)	9.6	6.2 [3.84;8.58]	<0.001
	Placebo (78)	3.3	-	-
9 g (Week 13)	LUMRYZ (68)	10.8	6.1 [3.52;8.75]	<0.001
	Placebo (78)	4.7	-	-

*Mean MWT at baseline was 5.0 minutes for the LUMRYZ group and 4.7 minutes for the placebo group

Table 4: Proportion of Patients with a Very Much or Much Improved Clinical Global Impression-Improvement

Dose	Treatment Group (N)	Percentage of Responders (Much or Very Much Improved)	Odds Ratio [95% CI]	p-value
6 g (Week 3)	LUMRYZ (87)	40	10.3 [3.93;26.92]	<0.001
	Placebo (87)	6	-	-
7.5 g (Week 8)	LUMRYZ (75)	64	5.7 [2.82;11.40]	<0.001
	Placebo (81)	22	-	-
9 g (Week 13)	LUMRYZ (69)	73	5.6 [2.76;11.23]	<0.001
	Placebo (79)	32	-	-

Table 5: Change from Baseline in the Mean Cataplexy Attacks Per Week in NT1 Patients

Dose	Treatment Group (N)	Change from Baseline*	Difference from Placebo [95% CI]	p-value
6 g (Week 3)	LUMRYZ (73)	-7.4	-4.8 [-7.03;-2.62]	<0.001
	Placebo (72)	-2.6	-	-
7.5 g (Week 8)	LUMRYZ (66)	-10.0	-6.3 [-8.74;-3.80]	<0.001
	Placebo (69)	-3.7	-	-

Dose	Treatment Group (N)	Change from Baseline*	Difference from Placebo [95% CI]	p-value
9 g (Week 13)	LUMRYZ (55)	-11.5	-6.7 [-9.32;-3.98]	<0.001
	Placebo (62)	-4.9	-	-

*Mean (SD) number of cataplexy attacks per week at baseline was 18.9 (8.7) in the LUMRYZ group and 19.8 (8.9) in the placebo group

14.2 Cataplexy and Excessive Daytime Sleepiness (EDS) in Pediatric Narcolepsy

The effectiveness of LUMRYZ in pediatric patients is based upon a clinical study in patients treated with immediate-release sodium oxybate, as described below.

The effectiveness of immediate-release sodium oxybate in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy was established in a double-blind, placebo-controlled, randomized-withdrawal study (NCT02221869). The study was conducted in 106 pediatric patients (median age: 12 years; range: 7 to 17 years) with a baseline history of at least 14 cataplexy attacks in a typical 2-week period prior to any treatment for narcolepsy symptoms. Of the 106 patients, 2 did not receive study drug and 63 patients were randomized 1:1 either to continued treatment with immediate-release sodium oxybate or to placebo. Randomization to placebo was stopped early as the efficacy criterion was met at the pre-planned interim analysis.

Patients entered the study either taking a stable dosage of immediate-release sodium oxybate or were immediate-release sodium oxybate-naïve. CNS stimulants were allowed at entry, and approximately 50% of patients continued taking a stable dose of stimulant throughout the stable-dose and double-blind periods. Immediate-release sodium oxybate-naïve patients were initiated and titrated based on body weight over a period of up to 10 weeks. The total nightly dose was administered in two divided doses, with the first dose given at nighttime and the second given 2.5 to 4 hours later. Once a stable dosage of immediate-release sodium oxybate had been achieved, these patients entered the 2-week stable-dose period; patients on a stable dosage of immediate-release sodium oxybate at study entry remained on this dosage for 3 weeks prior to randomization. Efficacy was established at dosages ranging from 3 g to 9 g of immediate-release sodium oxybate per night.

The primary efficacy measure was the change in frequency of cataplexy attacks. In addition, change in cataplexy severity was evaluated with the Clinical Global Impression of Change for cataplexy severity. The Clinical Global Impression of Change is evaluated on a 7-point scale, centered at No Change, and ranging from Very Much Worse to Very Much Improved. The efficacy of immediate-release sodium oxybate in the treatment of excessive daytime sleepiness in pediatric patients with narcolepsy was evaluated with the change in the Epworth Sleepiness Scale (Child and Adolescent) score. The Epworth Sleepiness Scale (Child and Adolescent) is a modified version of the Epworth Sleepiness Scale used in the adult clinical trial with immediate-release sodium oxybate. The Epworth Sleepiness Scale is intended to evaluate the extent of sleepiness in everyday situations by asking the patient a series of questions. In these questions, patients were asked to rate their chances of dozing during each of 8 activities on a scale from 0-3 (0=never; 1=slight; 2=moderate; 3=high). Higher total scores indicate a greater tendency to

sleepiness. The overall change in narcolepsy condition was assessed by the Clinical Global Impression of Change for narcolepsy overall. Efficacy was assessed during or at the end of the 2-week double-blind treatment period, relative to the last 2 weeks or end of the stable-dose period (see Tables 6 and 7).

Pediatric patients taking stable dosages of immediate-release sodium oxybate who were withdrawn from immediate-release sodium oxybate treatment and were randomized to placebo during the double-blind treatment period experienced a statistically significant increase in weekly cataplexy attacks compared with patients who were randomized to continue treatment with immediate-release sodium oxybate. Patients randomized to receive placebo during the double-blind treatment period experienced a statistically significant worsening of EDS compared with patients randomized to continue receiving immediate-release sodium oxybate (see Table 6).

Table 6: Number of Weekly Cataplexy Attacks and Epworth Sleepiness Scale (Child and Adolescent) Score

Treatment Group	Baseline^{*,†}	Double-blind Treatment Period^{‡,§}	Median Change from Baseline	Comparison to Placebo (p-value[¶])
Median Number of Cataplexy Attacks (attacks/week)				
Placebo (n=32)	4.7	21.3	12.7	-
Immediate-release Sodium Oxybate (n=31)	3.5	3.8	0.3	<0.0001
Median Epworth Sleepiness Scale (Child and Adolescent) Score				
Placebo (n=31 ^{**})	11	12	3	-
Immediate-release Sodium Oxybate (n=30 ^{**})	8	9	0	0.0004

* For weekly number of cataplexy attacks, baseline value is calculated from the last 14 days of the stable-dose period.

† For Epworth Sleepiness Scale score, baseline value is collected at the end of stable-dose period.

‡ Weekly number of cataplexy attacks is calculated from all days within the double-blind treatment period.

§ For Epworth Sleepiness Scale, value is collected at the end of the double-blind treatment period.

¶ P-value from rank-based analysis of covariance (ANCOVA) with treatment as a factor and rank baseline value as a covariate.

** One patient in each of the treatment groups did not have baseline ESS score available and were not included in this analysis.

Patients randomized to receive placebo during the double-blind treatment period experienced a statistically significant worsening of cataplexy severity and narcolepsy overall according to the clinician's assessment compared with patients randomized to continue receiving immediate-release sodium oxybate (see Table 7).

Table 7: Clinical Global Impression of Change (CGIc) for Cataplexy Severity and Narcolepsy Overall

Worsened, %[†]	CGIc Cataplexy Severity[*]	CGIc Narcolepsy Overall[*]

	Placebo (n=32)	Immediate-release Sodium Oxybate (n=29) [‡]	Placebo (n=32)	Immediate-release Sodium Oxybate (n=29) [‡]
Much worse or very much worse	66%	17%	59%	10%
p-value[§]	0.0001		<0.0001	

* Responses indicate change of severity or symptoms relative to receiving immediate-release sodium oxybate treatment at baseline.

† Percentages based on total number of observed values.

‡ Two patients randomized to immediate-release sodium oxybate did not have the CGIC assessments completed and were excluded from the analysis.

§ P-value from Pearson's chi-square test.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

LUMRYZ is a blend of white to off-white granules for extended-release oral suspension in water. LUMRYZ is supplied in cartons and a 28-day starter pack.

Cartons: each carton contains either 7 or 30 packets of LUMRYZ, a mixing cup, Prescribing Information and Medication Guide, and Instructions for Use (see Table 8). Dose packets contain a single dose of LUMRYZ provided in 4.5 g, 6 g, 7.5 g, or 9 g doses.

Table 8: LUMRYZ Carton Configurations

Strength	Package Size	NDC Number
4.5 g	7 packets	NDC 13551-001-07
	30 packets	NDC 13551-001-30
6 g	7 packets	NDC 13551-002-07
	30 packets	NDC 13551-002-30
7.5 g	7 packets	NDC 13551-003-07
	30 packets	NDC 13551-003-30
9 g	7 packets	NDC 13551-004-07
	30 packets	NDC 13551-004-30

28-day Starter Pack: contains four 7-count cartons, each containing a mixing cup, Prescribing Information and Medication Guide, and Instructions for Use (see Table 9). Dose packets contain a single dose of LUMRYZ provided in 4.5 g, 6 g, or 7.5 g doses.

Table 9: LUMRYZ Starter Pack Contents

28-day Starter Pack	Strength	Package Size	NDC Number
Week 1	4.5 g	7 packets	NDC 13551-005-01
Week 2	6 g	7 packets	
Week 3	6 g	7 packets	
Week 4	7.5 g	7 packets	

16.2 Storage

Keep out of reach of children.

LUMRYZ should be stored at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature).

Suspensions should be consumed within 30 minutes.

16.3 Handling and Disposal

LUMRYZ is a Schedule III drug under the Controlled Substances Act. LUMRYZ should be handled according to state and federal regulations. It is safe to dispose of LUMRYZ down the sanitary sewer.

17 PATIENT COUNSELING INFORMATION

Advise the patient and/or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Central Nervous System Depression

Inform patients and/or caregivers that LUMRYZ can cause central nervous system depression, including respiratory depression, hypotension, profound sedation, syncope, and death. Instruct patients to not engage in activities requiring mental alertness or motor coordination, including operating hazardous machinery, for at least 6 hours after taking LUMRYZ. Instruct patients and/or caregivers to inform their healthcare providers of all the medications they take [see *Warnings and Precautions* (5.1)].

Abuse and Misuse

Inform patients and/or caregivers that the active ingredient of LUMRYZ is gamma-hydroxybutyrate (GHB), which is associated with serious adverse reactions with illicit use and abuse [see *Warnings and Precautions* (5.2)].

LUMRYZ REMS

LUMRYZ is available only through a restricted program called the LUMRYZ REMS [see *Warnings and Precautions (5.3)*]. Inform the patient and/or caregiver of the following notable requirements:

- LUMRYZ is dispensed only by pharmacies that are specially certified
- LUMRYZ will be dispensed and shipped only to patients who are enrolled in the LUMRYZ REMS

LUMRYZ is available only from certified pharmacies participating in the program. Therefore, provide patients and/or caregivers with the telephone number and website for information on how to obtain the product.

Alcohol or Sedative Hypnotics

Advise patients and/or caregivers that alcohol and other sedative hypnotics should not be taken with LUMRYZ [see *Contraindications (4) and Warnings and Precautions (5.1)*].

Sedation

Inform patients and/or caregivers that they are likely to fall asleep quickly after taking LUMRYZ (often within 5 and usually within 15 minutes), but the time it takes to fall asleep can vary from night to night. The sudden onset of sleep, including in a standing position or while rising from bed, has led to falls complicated by injuries, in some cases requiring hospitalization [see *Adverse Reactions (6.2)*]. Instruct patients and/or caregivers that they should remain in bed following ingestion of their dose [see *Dosage and Administration (2.3)*].

Food Effects on LUMRYZ

Inform patients and/or caregivers that LUMRYZ should be taken at least 2 hours after eating.

Respiratory Depression and Sleep-Disordered Breathing

Inform patients and/or caregivers that LUMRYZ may impair respiratory drive, especially in patients with compromised respiratory function, and may cause apnea [see *Warnings and Precautions (5.4)*].

Depression and Suicidality

Instruct patients and/or caregivers to contact a healthcare provider immediately if they develop depressed mood, markedly diminished interest or pleasure in usual activities, significant change in weight and/or appetite, psychomotor agitation or retardation, increased fatigue, feelings of guilt or worthlessness, slowed thinking or impaired concentration, or suicidal ideation [see *Warnings and Precautions (5.5)*].

Other Behavioral or Psychiatric Adverse Reactions

Inform patients and/or caregivers that LUMRYZ can cause behavioral or psychiatric adverse reactions, including confusion, anxiety, and psychosis. Instruct them to notify their healthcare provider if any of these types of symptoms occur [see *Warnings and Precautions (5.6)*].

Sleepwalking

Instruct patients and/or caregivers that LUMRYZ has been associated with sleepwalking and other behaviors during sleep, and to contact their healthcare provider if this occurs [see *Warnings and Precautions (5.7)*].

Sodium Intake

Instruct patients and/or caregivers that LUMRYZ contains a significant amount of sodium and patients who are sensitive to sodium intake (e.g., those with heart failure, hypertension, or renal impairment) should limit their sodium intake [see *Warnings and Precautions (5.8)*].

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