IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC., Plaintiff, v. AVADEL CNS PHARMACEUTICALS LLC, Defendant.	)	**PUBLIC VERSION** C.A. No. 21-691 (GBW) [redacted]
JAZZ PHARMACEUTICALS, INC. and JAZZ PHARMACEUTICALS IRELAND LIMITED, Plaintiffs, v. AVADEL CNS PHARMACEUTICALS LLC, Defendant.	)	 C.A. No. 21-1138 (GBW) [redacted]
JAZZ PHARMACEUTICALS, INC. and JAZZ PHARMACEUTICALS IRELAND LIMITED, Plaintiffs, v. AVADEL CNS PHARMACEUTICALS LLC, Defendant.	)	 C.A. No. 21-1594 (GBW) [redacted]

PLAINTIFFS' REPLY BRIEF IN SUPPORT OF MOTION FOR A PERMANENT INJUNCTION AND FOR AN ONGOING ROYALTY

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[1] All D.I. cites refer to the docket in Case No. 21-cv-00691-GBW unless otherwise specified.

Document	**Citation**
Lumryz Adverse Events reported to the U.S. Food and Drug Administration's Adverse Event Reporting System ("FAERS"), searchable at https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard	"Ex. 23"
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Morse, A.M., et al., *Dosing Optimization of Low-Sodium Oxybate in Narcolepsy and Idiopathic Hypersomnia in Adults: Consensus Recommendations*, Neurol Ther. 2024 Apr 25	"Ex. 27"
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Bruck, D. and Parkes, J.D., *A comparison of idiopathic hypersomnia and narcolepsy-cataplexy using self report measures and sleep diary data*, JNNP 60:576-578 (1999)	"Ex. 30"
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D.I. 601, Exhibit 6, Jazz Pharms. Form 10-Q (May 2, 2024)	Op., Ex. 6

This is not about whether Avadel should be permitted to market *any* once-nightly oxybate. Instead, this is about whether Avadel should be permitted to continue infringing the *specific* formulation of claim 24. Avadel does not dispute that its patents disclose formulations that do *not* infringe claim 24. Instead, Avadel chooses to infringe; it doubles down on using Jazz's innovation to target Jazz's patients to switch to Lumryz™ through the '782 patent's expiry in 2036, including by seeking to expand Lumryz's label to include an IH indication. No court has denied an injunction when such facts are present. This Court should not be the first.

I. An Injunction Would Not Disserve The Public Interest

The requested injunction "strikes a workable balance between protecting the patentee's rights and protecting the public from the injunction's adverse effects." *i4i Ltd. P'ship v. Microsoft Corp.*, 598 F.3d 831, 863 (Fed. Cir. 2010), *aff'd*, 564 U.S. 91 (2011). Avadel's claim that Lumryz is a "sea change" that must be put above Jazz's rights (Op. at 3), is baseless.

First, Lumryz does not give a better "chance to get an undisturbed night's sleep" than Jazz's products. *Id.* Instead, data shows that both parties' products similarly reduce the number of narcolepsy nighttime awakenings from about 80 to about 40. Exs. 20-22; Bogan ¶¶28-29.

Second, Jazz did not "ignore[]" or "belittle[]" Lumryz's alleged clinical superiority. Op. at 5-7. Instead, Jazz explained the alleged superiority is limited to non-salt-sensitive narcolepsy patients only. Br. at 15-16. Avadel ignores data showing that most patients do not fall within the FDA's limited finding. *Id.* at 16. Instead, Avadel misleadingly quotes JTX112 to proclaim, like it does to the detriment of Jazz's reputation and goodwill, that "once-nightly dosing would outweigh the risk of increased sodium intake." Op. at 6. It does not say that. *See* Br. 15-16.

Third, unlike in the cases Avadel cites (*Id.* at 7), Lumryz is not safer or more effective than Jazz's products (Bogan ¶¶26-34), nor is it life-saving. Despite Avadel's protest (Op. at 6), FDA

rejected Avadel's claim that Lumryz provides "greater safety . . . over either Xyrem or Xywav" (JTX112.28), and instead found "Lumryz raises the same safety concern that was present for Xyrem [] that is not present for Xywav" (JTX112.32). FDA also found "[t]here is no evidence suggesting that the efficacy of Lumryz is different from that of Xyrem or Xywav" JTX112.28, let alone any better. In fact, the same alleged side effects of Jazz's products exist for Lumryz. Of 1700 Lumryz prescriptions so far, ~630 adverse events have been reported to FDA, including ~120 reports of missed/wrong doses, 300+ reports of insomnia/drug ineffectiveness, 44 reports of anxiety, and 13 reports of weight increase/hunger. Ex. 23; Bogan ¶¶32-34.

Fourth, Avadel's declarations—which (unlike Jazz's) come from undisclosed witnesses who were not subject to cross examination[2]—do not establish that the injunction would disserve the public interest. Declarations from three HCPs (of 1,600+ oxybate HCPs) "regarding their personal preferences . . . cannot be interpreted and cited as though [they] represent[] that of the majority of doctors." *Mallinckrodt, Inc. v. Masimo Corp.*, 147 F. App'x 158, 177 (Fed. Cir. 2005).[3] The declarants have relationships with Avadel. Ex. 24 at 53-54, 156-157; Ex. 25. And all but 1 patient do not say how long they have taken Lumryz or say that it has been no more than 6 months. Patients' opinions on drugs change over time. *See* Patient 2, ¶ 6; Patient 3, ¶ 5.

NP Lavender states that narcolepsy is well controlled with Jazz's products and switching to Lumryz is about patient choice. Lavender, ¶¶ 15-17. "But eliminating a choice of drugs is not, by itself, sufficient to disserve the public interest." *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1381 (Fed. Cir. 2017); *see also WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1343 (Fed. Cir. 2016). That is especially true where Avadel has told the world it has alternative formulations that do not

[2] Avadel's declarations violate at least FRCP 26 and FRE 701, 702, 801, and 802, and should not be considered. Jazz submits Kryger and Bogan to the extent they are considered.

[3] Although pre-*eBay*, the court still weighed the public interest factor.

infringe claim 24. Br. at 12-13; *Transamerica Life Ins. v. Lincoln Nat. Life Ins.*, 625 F. Supp. 2d 702, 719-21 (N.D. Iowa 2009), *rev'd on validity grounds*, 609 F.3d 1364 (Fed. Cir. 2010); *SynQor, Inc v. Artesyn Techs*, No. 07-497, 2011 WL 238645, at *5-6 (E.D. Tex. Jan. 24, 2011).

Fifth, Lumryz has no advantage over Xywav for IH. Xywav is approved once-nightly for IH. Citing only Dr. Stern's say-so, Avadel claims the "vast majority of IH patients take [Xywav] twice nightly." Op. at 9. There are 3,000+ IH patients on Xywav, yet Dr. Stern does not provide any evidence on how many Xywav or IH patients he treats, let alone that it is the vast majority of both. FDA approved once-nightly Xywav as safe and effective for IH and a peer-reviewed publication concludes that once-nightly dosing shows "similar" efficacy to twice-nightly. Ex. 26 at 63, supp. Appendix p. 2; Bogan ¶24. And the separate FDA-labeled-indications and clinical study requirements disprove Avadel's argument that IH and narcolepsy are not "distinct diseases." Op. at 9. So do peer-reviewed papers. Exs. 27-31; Bogan ¶¶13-18; Kryger ¶¶7-9.

II. Jazz Established Irreparable Harm And Inadequacy Of Monetary Damages

First, Jazz established causal nexus. Claim 24 adds much more to the prior art than "sachet packaging." Op. at 11-13. Avadel does not dispute that claim 24 covers Lumryz as a whole. And unrebutted testimony shows that the invention is what makes a modified/immediate release oxybate formulation administrable and stable. Tr. at 155:9-157:2. If Lumryz were not administrable and stable, the FDA would not have approved it and no one would buy it. Avadel mischaracterizes claim 24 and the nexus law. Br. at 9-10; *cf. AstraZeneca AB v. Apotex Corp.*, 782 F.3d 1324, 1337-40 (Fed. Cir. 2015) (pharmaceutical formulation is a driver of sales).

Second, Jazz's public statements do not contradict its proof of irreparable harm. Avadel does not dispute that it is purposefully targeting Jazz's patients and taking market share, nor does the improper Rao declaration. The patients Avadel "switch[es]" are different from patients who

discontinued Jazz's products. Ex. 32; Ex. 33 at 30. And while data Avadel relies on shows that Xywav sales increased Q1'23 to Q1'24, they did not increase as much as Xyrem sales decreased, which had been the trend before. Op., Ex. 6 at 27; Tr. 128:16-130:4; Ex. 5 at 80; Ex. 4 at 83. [redacted] and further harm Jazz's market share. Jazz suffered price erosion as a direct result of Lumryz's launch. Br. at 6-7.

Third, unlike in *Advanced Cardiovascular* (Op. at 15), Jazz has never licensed the patent-in-suit. Jazz's decision to license unrelated patents covering Xyrem and Xywav to settle litigation is irrelevant. *Acumed LLC v. Stryker Corp.*, 551 F.3d 1323, 1327-1329 (Fed. Cir. 2008). And contrary to Avadel's argument (Op. at 15-16), the Federal Circuit "ha[s] never held . . . that in order to establish irreparable harm a patentee must demonstrate that it is entitled to lost profits." *Mytee Prods. v. Harris Rsch.*, 439 F. App'x 882, 887 (Fed. Cir. 2011).

Fourth, despite Avadel's claim (Op. at 16), practicing the invention is not a prerequisite for irreparable reputational harm, especially where the parties are direct competitors. *Natera Inc. v. ArcherDx, Inc.*, No. 20-125, 2023 WL 9103876, at *3-4 (D. Del. Dec. 1, 2023). Nor is consumer confusion. *Douglas Dynamics, LLC v. Buyers Prods. Co.*, 717 F.3d 1336, 1344-45 (Fed. Cir. 2013). And, notably, Avadel does not deny the bases for Jazz's reputational harm.

III. The Balance Of Hardships Favors Jazz

Avadel refuses to take blame for its own poor decision-making. Br. at 11-13. It claims the [redacted] (Op. at 10, 17-18), but Avadel was pleased with its net revenue in Q1'24 (Ex. 33 at 11). [redacted] 82.7% increase in year-over-year spending, including "higher compensation and legal costs." *Id.* at 11-12. That could be cured by taking less pay, staying various litigations with Jazz, or not infringing. And in *Bio-Rad* and *Hynix*, unlike here, there was specific evidence of why possible non-infringing alternatives were not used. *Bio-Rad*, 967 F.3d at 1378-79; *Hynix*, 609 F. Supp. 2d at 985; Br. at 11-12.

IV. Avadel Waived Its Unclean Hands Argument, And It Lacks Merit Regardless

The unclean hands defense Avadel now offers was never pled and is waived. *Bench Walk Lighting v. Everlight Electronics Co.*, No. 20-49, 2020 WL 5128086, at *1-2 (D. Del. Aug. 31, 2020). Regardless, it lacks merit. *See* C.A. No. 21-941, D.I. 22, 28, 48, 56, 80, 84.

V. Jazz's Ongoing Royalty Is The Correct One

Avadel ignores case law (Br. at 19-20) that supports this Court's authority to award an ongoing royalty rate greater than the jury's 3.5% rate for past infringement.[4] Avadel also does not dispute that it stands to make billions under Jazz's requested rates, that it has no plans to launch a non-infringing alternative, and that it presented the jury with its argument that the validity of the claim 24 was uncertain as of the hypothetical negotiation. *Id*. at 18-20; D.I. 589.

The jury's 3.5% royalty rate is not "a fully-paid-up royalty." Op. at 19-20. The jury awarded damages for "Avadel's *past* infringement" using "*Past* Sales." D.I. 579, at 11 (emphasis added). The jury also did not "apportion" damages to "20% of sales of Lumryz." It mistakenly used Lumryz [redacted] $6,673,223.82—*down to the exact penny*. *Compare* Ex. 34 (Col. F, Row 54) with D.I. 579 at 11.[5] Lumryz was not reformulated to be non-infringing after that date and claim 24 covers Lumryz as a whole. JTX-0006.19; Tr. 585:5-17, 605:17-21, 606:7-17; *AstraZeneca*, 782 F.3d at 1337-38. Thus, there is no legal basis to award a lower royalty rate than Jazz requests, award an ongoing royalty based on "some fraction of Lumryz sales," or to "decline to award any ongoing royalty" (Op. at 20).

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[4] Because Jazz will fully address the jury's legally insufficient damages award in upcoming post-trial motions, Jazz reserves the right to further address the ongoing royalty if needed.

[5] $6,673,223.82 [redacted] ÷ $32,519,345 (*net* sales through Jan. 31, 2024) = 20.52078176851348%. If anything, this shows that the jury credited *gross* sales (rather than net sales) as the appropriate base for past damages. The gross sales of Lumryz through January 31, 2024 as presented to the jury totaled [redacted] Ex. 35 (Col. F, Row 54).

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jeremy A. Tigan

Jack B. Blumenfeld (#1014)
Jeremy A. Tigan (#5239)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899
(302) 658-9200
jblumenfeld@morrisnichols.com
jtigan@morrisnichols.com

Attorneys for Plaintiffs
Jazz Pharmaceuticals, Inc. and
Jazz Pharmaceuticals Ireland Limited

OF COUNSEL:

F. Dominic Cerrito
Eric C. Stops
Evangeline Shih
Andrew S. Chalson
Gabriel P. Brier
Frank C. Calvosa
Nicholas A. LoCastro
Krista M. Rycroft
Quentin Jorgensen
Catherine T. Mattes
Abigail DeMasi
Elizabeth J. Murphy
Raymond N. Nimrod
Ellyde R. Thompson
Brian J. Forsatz, Ph.D.
Shannon Prince
Shira Bergman
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
51 Madison Avenue, 22nd Floor
New York, NY 10010
(212) 849-7000

Alexandra Kim
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
111 Huntington Ave., Suite 520
Boston, MA 02199
(617) 712-7100

Christopher D. Porter
Elizabeth M. Devaney
QUINN EMANUEL URQUHART
& SULLIVAN, LLP
Pennzoil Place
711 Louisiana Street, Suite 500
Houston, TX 77002
(713) 221-7000

May 20, 2024

CERTIFICATE OF SERVICE

I hereby certify that on May 20, 2024, 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 May 20, 2024, upon the following in the manner indicated:

Daniel M. Silver, Esquire — *VIA ELECTRONIC MAIL*
Alexandra M. Joyce, Esquire
McCARTER & ENGLISH, LLP
Renaissance Centre
405 N. King Street, 8th Floor
Wilmington, DE 19801
Attorneys for Defendant

Kenneth G. Schuler, Esquire — *VIA ELECTRONIC MAIL*
Marc N. Zubick, Esquire
Alex Grabowski, Esquire
Sarah W. Wang, Esquire
Laryssa Bedley, Esquire
Michelle Chin, Esquire
LATHAM & WATKINS LLP
330 North Wabash Avenue, Suite 2800
Chicago, IL 60611
Attorneys for Defendant

Herman H. Yue, Esquire — *VIA ELECTRONIC MAIL*
Franco Benyamin, Esquire
Ramya Sri Vallabhaneni, Esquire
LATHAM & WATKINS LLP
1271 Avenue of the Americas
New York, NY 10020
Attorneys for Defendant

Audra Sawyer, Esquire
Alan J. Devlin, Esquire
Ian Conner, Esquire
Denise Laspina, Esquire
Kelly Welsh, Esquire
LATHAM & WATKINS LLP
555 Eleventh Street, NW, Suite 1000
Washington, D.C. 20004-1304
Attorneys for Defendant

VIA ELECTRONIC MAIL

Daralyn J. Durie, Esquire
Eric P. Berger, Esquire
Rebecca E. Weires, Esquire
Adam R. Brausa, Esquire
Tannyr Pasvantis, Esquire
Umeet K. Sajjan, Esquire
MORRISON & FOERSTER LLP
425 Market Street
San Francisco, CA 94105
Attorneys for Defendant

VIA ELECTRONIC MAIL

Kira A. Davis, Esquire
Henry Huttinger, Esquire
Katherine E. McNutt, Esquire
Rose S. Lee, Esquire
MORRISON & FOERSTER LLP
707 Wilshire Boulevard
Los Angeles, CA 90017
Attorneys for Defendant

VIA ELECTRONIC MAIL

David F. McGowan, Esquire
David F. Kowalski, Esquire
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, CA 92130
Attorneys for Defendant

VIA ELECTRONIC MAIL

Andrew T. Jones, Esquire
MORRISON & FOERSTER LLP
2100 L Street, NW, Suite 900
Washington, D.C. 20037
Attorneys for Defendant

VIA ELECTRONIC MAIL

Scott F. Llewellyn, Esquire
MORRISON & FOERSTER LLP
4200 Republic Plaza
370 Seventeenth Street
Denver, CO 80202-5638
Attorneys for Defendant

VIA ELECTRONIC MAIL

/s/ Jeremy A. Tigan

Jeremy A. Tigan (#5239)