IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

JAZZ PHARMACEUTICALS, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. 21-691 (MN)
	)	
AVADEL CNS PHARMACEUTICALS LLC,	)	[redacted]
	)	
Defendant.	)	REDACTED - PUBLIC VERSION

PLAINTIFF'S ANSWERING BRIEF IN OPPOSITION TO DEFENDANT'S RENEWED MOTION FOR PARTIAL JUDGMENT ON THE PLEADINGS

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I. NATURE AND STAGE OF THE PROCEEDINGS

This is a Hatch-Waxman and declaratory judgment patent-infringement action between Plaintiff Jazz Pharmaceuticals, Inc. ("Jazz") and Defendant Avadel CNS Pharmaceuticals, LLC ("Avadel"). There are five patents-in-suit. Only one patent—U.S. Patent No. 8,731,963 (the "'963 patent")—is in dispute in Avadel's motion.[1]

In the Complaint, Jazz pled that the '963 patent covers "methods of use and administration of sodium oxybate." D.I. 1 at ¶ 27; *see also id.* at ¶¶ 29-30 (pleading that the '963 patent covers Jazz's XYWAV™ and XYREM® REMS programs). In its Answer, Avadel disagreed that the '963 patent "claim[s] a method of using the approved drug product as required by 21 C.F.R. § 314.53(c) and thus should be removed from the Orange Book." D.I. 11 at ¶¶ 25-31 (the "Delisting Counterclaim"). On July 23, 2021, Avadel moved for partial judgment on the pleadings for its Delisting Counterclaim (D.I. 20 & 21), which Jazz opposed on August 20, 2021 (D.I. 43). On October 19, 2021, the Court denied Avadel's motion based, in part, on the need to decide *Markman* (i.e., whether the '963 patent claims methods or computer systems) before deciding Avadel's Delisting Counterclaim. D.I. 55 & 56.

On June 23, 2022, before *Markman* briefing and adjudication were completed, and without the requisite leave of Court required by the operative Scheduling Order (*see* D.I. 120; D.I. 31 at ¶ 15), Avadel filed a "renewed" motion for partial judgment on the pleadings for its Delisting Counterclaim (D.I. 117 & 118). On July 7, 2022, Jazz objected to Avadel's "renewed" motion as premature and procedurally improper. D.I. 124. On August 24, the Court ordered "that, by no

[1] Two additional patents are in-suit in C.A. Nos. 21-1138 and 21-1594, which are coordinated with the present action. D.I. 65. Those patents are also not implicated by Avadel's motion.

later than 6:00 PM on 8/26/2022, [Jazz] shall file a response on the merits to the Renewed Motion for Judgment on the Pleadings." D.I. 151. This opposition follows.

II. SUMMARY OF ARGUMENT

In its renewed motion, Avadel argues that the '963 patent must be delisted from the Orange Book regardless of whether it claims methods or computer systems. Avadel is mistaken. Delisting is improper under either construction.

First, if the Court rules that the '963 patent claims methods, then Jazz was ***required*** to list it in the Orange Book and delisting would be improper. The applicable statute and regulations require innovator pharmaceutical companies that file a New Drug Application ("NDA")—like Jazz—to submit for listing in the Orange Book any patent claiming a method of using the drug that is the subject of the NDA. Importantly, method-of-use patents include not only those that claim therapeutic indications, but also those that claim "other conditions of use" for which approval is sought or has been granted in the NDA. 21 C.F.R. § 314.53(b)(1). When the FDA first approved Jazz's sodium oxybate drug product (Xyrem®), it expressly conditioned approval on Jazz marketing the drug in accordance with the specific restrictions on distribution and use that are claimed in the '963 patent. Thus, there can be no doubt that the '963 patent claims a condition of use for which approval was granted (consistent with the Use Code), and therefore that the patent was required to be listed in the Orange Book in connection with Xyrem®. In fact, ***the FDA recently confirmed this*** when it required Avadel to submit an appropriate patent certification for the '963 patent.[2] Avadel argues that Jazz's *Markman* position somehow evidences that the '963 patent claims "[a] method of using a system for distribution . . . not a 'method of using [a] drug.'" D.I.

[2] Avadel is simultaneously challenging the FDA's requirement before the District Court for the District of Columbia. *See* D.I. 138.

118 at 2. Avadel is again mistaken; as explained below, its position is based on a mischaracterization and selective reading of Jazz's position.

Second, if the Court rules that the '963 patent claims computer systems, then Jazz was ***permitted*** to list it in the Orange Book and delisting would remain improper. Avadel's counterargument is based on a provision of the Hatch-Waxman Act that ***was not enacted until nearly 7 years after*** the '963 patent was listed in the Orange Book. That provision, by law, cannot be applied retroactively; thus, Avadel's Delisting Counterclaim fails. Importantly, even were the Court to apply the statute retroactively, delisting should still not be granted; under FDA regulations, Jazz has 30 days to correct any patent listing that is affected by order of a District Court ***without*** that correction having any impact on Avadel's patent certification.[3]

For these reasons and as explained further below, Avadel's motion should be denied.

III. STATEMENT OF FACTS

A. Xyrem® was approved with mandatory conditions of use that are covered by the '963 patent

Jazz developed and markets Xyrem®, an FDA-approved drug product for use in the treatment of both cataplexy and excessive daytime sleepiness, which are devastating symptoms associated with the sleep disorder narcolepsy. *See, e.g.*, D.I. 1, Ex. B at 2:51-55.

The active ingredient in Xyrem® is sodium oxybate, which is a specific salt form of gamma-hydroxybutyrate ("GHB"). *Id.* GHB has been recognized by Congress and federal agencies as a dangerous substance, frequently misused as a "date rape drug" in cases of drug-

[3] Should such correction become necessary, Jazz would likely seek leave to amend its Complaint. Because the Court has not yet adjudicated *Markman*, however, any such request would be premature and seek an improper advisory opinion from this Court. *See Hines on behalf of Sevier v. Sec'y of Dep't of Health & Hum. Servs.*, 940 F.2d 1518, 1522 (Fed. Cir. 1991) ("Article III of the U.S. Constitution . . . has been interpreted as barring federal courts from rendering advisory opinions.") (citing *Aetna Life Ins. Co. v. Haworth*, 300 U.S. 227, 240-41 (1937)).

facilitated sexual assault. Because of its high potential for abuse and misuse involving third parties, GHB was classified as a Schedule I controlled substance under the Controlled Substances Act, a designation reserved for drugs with a high potential for abuse and no accepted medical use. *See* 21 U.S.C. § 812(b)(1); 21 C.F.R. § 1308.11(e)(1). At the same time, however, the FDA and Congress recognized that studies had established that GHB might be the basis for a unique treatment for certain symptoms of narcolepsy. *See, e.g.*, D.I. 1, Ex. B at 1:41-58. Thus, FDA-approved forms of GHB—like Xyrem®—were classified as Schedule III controlled substances, acknowledging their legitimate medical uses. *See* 21 U.S.C. § 812(b)(3); 21 C.F.R. § 1308.13(c)(6). In reaching this compromise, however, both Congress and the FDA noted that medical use of a GHB-based drug—like Xyrem®—must be strictly controlled to ensure that it cannot be illicitly obtained and misused.

Given its unique status, the FDA conditioned approval of Xyrem® on Jazz's development and use of a controlled distribution program to ensure proper use of the drug. Specifically, upon FDA approval of Xyrem® in 2002, the FDA stated that the drug could only be "approved with a Risk Management Program (RMP) that must include [several specified] components." Ex. A at 2.[4,5] In fact, the FDA stated in Xyrem®'s approval letter in no uncertain terms that the "[m]arketing of this drug product and related activities are to be in accordance with the substance and procedure

[4] A REMS is a form of Risk Management Program that the FDA can require for certain medications with serious safety concerns to help ensure that the benefits of the medication outweigh its risks. *See, e.g.*, https://www.fda.gov/files/drugs/published/Risk-Evaluation-and-Mitigation-Strategies--Modifications-and-Revisions-Guidance-for-Industry.pdf at 2.

[5] The Court may take judicial notice of the FDA Approval Letter for Xyrem®, and other exhibits cited herein, which are publicly available on the FDA's website. *See, e.g.*, *Freed v. St. Jude Med., Inc.*, No. 17-1128, 2017 WL 4102583, at *2 (D. Del. Sept. 15, 2017) (taking judicial notice of documents "because they are publically available on the FDA's website and are indisputably authentic"); *Desai v. Sorin CRM USA, Inc.*, No. 12-2995, 2013 WL 163298, at *4 (D.N.J. Jan. 15, 2013) (explaining, in context of deciding a Rule 12(c) motion, that "[t]his Court takes judicial notice of the FDA's website").

of all FDA regulations ***and the specific restrictions on distribution and use described [in the Xyrem Risk Management Program] below***." *Id.* at 1 (emphasis added).

The FDA required the Xyrem Risk Management Program in 2002 as "restrictions to assure safe use" pursuant to the Subpart H rules, and specifically 21 C.F.R. § 314.520(a). The Subpart H regulations and their preambles specifically describe the restrictions imposed under Section 520 as approved conditions of use. *See* 21 C.F.R. § 314.520(a) ("If FDA concludes that a drug product shown to be effective can be safely used only if distribution or use is restricted, FDA will require such postmarketing restrictions as are needed to assure safe use of the drug product."). Thus, 21 C.F.R. § 314.530(a)(6) allows FDA to use expedited procedures to withdraw approval if a drug approved with Section 520 restrictions is no longer "safe or effective under its conditions of use." *See also* New Drug, Antibiotic, and Biological Drug Product Regulations; Accelerated Approval, 57 Fed. Reg. 58951 (Dec. 11, 1992) ("[T]he restrictions contemplated under [§ 314.520] are precisely those deemed necessary to ensure that section 505 criteria have been met, i.e., restrictions to ensure that the drug will be safe under its approved conditions of use."); *id.* ("The restrictions under these provisions would be imposed on the sponsor only as necessary for safe use under the extraordinary circumstances of the particular drug and use. Without such restrictions, the drugs would not meet the statutory criteria, could not be approved for distribution, and would not be available for prescribing or dispensing."); *id.* at 53952 ("The burden is on the applicant to ensure that the conditions of use under which the applicant's product was approved are being followed.").

Following FDA approval, the package insert for Xyrem® specifies that "Xyrem is available only through a restricted distribution program called the XYWAV and XYREM REMS because of the risks of central nervous system depression and abuse and misuse." *See, e.g.*, Ex. B at § 5.3

and Black Box Warning.[6] Consequently, distributing and using Xyrem® according to the methods set forth in the FDA-required REMS (which are covered by the '963 patent) are conditions of using the drug.

B. The '963 patent covers the methods of use required by the Xyrem® REMS

The claims of the '963 patent address the unique problem that the Xyrem® REMS was invented to solve: using GHB for legitimate medical purposes while avoiding the potential for misuse, abuse, or diversion of GHB by or against others. *See* D.I. 1, Ex. A at 1:32-45. The claims cover methods of using a computer-implemented system to safely distribute GHB for treatment of a narcoleptic patient. Specifically, the independent claims recite a "computer-implemented system for treatment of a narcoleptic patient with a prescription drug that has a potential for misuse, abuse or diversion . . . ." *See, e.g.*, *id.* at Claim 1.

Jazz explained why the '963 patent is directed to methods in its *Markman* briefing. D.I. 132 at 46-49, 57-62. Avadel bases its motion on that briefing. *See, e.g.*, D.I. 118 at 9. Put simply, the '963 patent claims the FDA-required conditions of using Xyrem® according to its labeling, including the REMS invented by Jazz. Accordingly, the '963 patent is properly listed in the Orange Book.

C. Avadel's cries of imminent "devastati[on]" ring hollow

Avadel describes its infringing sodium oxybate drug product as "revolutionary," and argues that "Avadel is not an ANDA applicant seeking to market a generic version of a brand name drug." D.I. 118 at 2. To make its argument, Avadel compares its once-nightly sodium oxybate formulation (which it calls "FT218," and which is also referred to in Avadel's NDA as Lumryz)

[6] Xywav® is an oxybate product marketed by Jazz that contains 92% less sodium than Xyrem® and is also distributed and used according to the methods set forth in the '963 patent. For simplicity's sake, the XYWAV and XYREM REMS is referred to here as the "Xyrem® REMS."

to Xyrem®, which is currently dosed twice nightly. *See id.* Avadel omits, however, that although Jazz has yet to bring a once-nightly sodium oxybate formulation to market, Jazz has been developing such a formulation for years and has obtained several patents that cover its innovations. In fact, four of the five patents in this case claim once-nightly sodium oxybate formulations, and Avadel's FT218 infringes them all. *See* D.I. 1, Exs. B-E.

Moreover, despite its claims of innovation, Avadel chose to seek FDA approval for FT218 via an abbreviated regulatory pathway by largely relying upon Jazz's innovative work with Xyrem®. Indeed, Avadel did not file a typical NDA, but instead submitted a 505(b)(2) NDA. *See, e.g.*, D.I. 1, Ex. F at 13. A 505(b)(2) NDA sponsor is permitted to "rely on clinical studies that were previously submitted to [the] FDA in support of another drug and that were not conducted or licensed by the 505(b)(2) [sponsor]." *Veloxis Pharms., Inc. v. U.S. Food & Drug Admin.*, 109 F. Supp. 3d 104, 108-09 (D.D.C. 2015) (alteration in original). In this case, Xyrem® is the Reference Listed Drug ("RLD") for Avadel's 505(b)(2) NDA. *See, e.g.*, D.I. 1, Ex. F at 12; *id.*, Ex. I at 7. The RLD-related clinical studies that a 505(b)(2) NDA sponsor relies upon may be submitted to satisfy the sponsor's "entire burden of proving safety and effectiveness" to the FDA. *Veloxis*, 109 F. Supp. 3d at 109. To that end, the 505(b)(2) NDA pathway is "often used when the new drug differs only slightly from the pioneer [or reference listed] drug." *Id.*

And although Avadel filed a 505(b)(2) NDA that relied upon Xyrem® as the RLD, as Avadel admits, it initially refused to file ***any*** patent certification with respect to the Orange Book-listed '963 patent. *See* D.I. 118 at 3. As Avadel notes, however, "[t]he FDA recently required that Avadel certify to the '963 patent . . . ." *Id.* Avadel could (and should) have filed that patent certification at least as early as December 2020 when it submitted its 505(b)(2) NDA, and has only itself to blame for not doing so. Despite this, Avadel now seeks to prejudice Jazz and burden the

Court by demanding "[e]xpeditious resolution" of its Delisting Counterclaim through baseless and repetitive motion practice. *Id.* at 4. Avadel claims that, because it chose to pursue an unsuccessful regulatory strategy at the FDA (i.e., ignoring the '963 patent altogether), and because a 30-month stay on potential approval of its NDA[7] is now in place until June 2023 (less than 10 months from now), there are allegedly "devastating" effects on Avadel's commercial viability. *See id.* at 4 ("Avadel . . . has no other currently marketed products that can fund its operations . . . ."). Avadel's claim is unsubstantiated; but even if accurate, it is a problem entirely of Avadel's own making. Indeed, along with its misguided regulatory strategy, Avadel made poor commercial decisions. Avadel "has been around for over 30 years," and throughout that time has had several revenue-generating products. Ex. D at 1. But from 2018-2020, Avadel made a decision to divest all such products and become "singularly focused on supporting the regulatory approval process, market planning and maximizing shareholder value for FT218." Ex. E. That Avadel's strategic risk did not bear fruit is not Jazz's fault.

IV. LEGAL STANDARD

Under Federal Rule of Civil Procedure 12(c), judgment on the pleadings "will not be granted unless the movant clearly establishes that no material issue of fact remains to be resolved and that he is entitled to judgment as a matter of law." *Rosenau v. Unifund Corp.*, 539 F.3d 218, 221 (3d Cir. 2008) (internal quotation marks and citations omitted). The court "must view the facts presented in the pleadings and the inferences to be drawn therefrom in the light most favorable to the nonmoving party." *Id.*; *see also, e.g.*, *Aqua Connect, Inc. v. TeamViewer US, LLC*, No. 18-1572 (MN), 2020 WL 5549086, at *1 (D. Del. Sept. 16, 2020) ("In ruling on a Rule

[7] Avadel's tentative approval letter states that it "does not address whether any orphan drug exclusivity (ODE) recognized for Xyrem . . . or for Xywav . . . affects the approvability of Avadel's application." Ex. C at 1 n.1.

12(c) motion, the Court must accept as true all well-pleaded allegations in the non-movant's pleadings and draw all reasonable inferences in favor of the non-movant.").

V. ARGUMENT

A. The '963 patent claims methods and Jazz was required to list it in the Orange Book

1. Jazz was required to the list the method claims in the Orange Book

Under the Hatch-Waxman Act, NDA holders were (and still are) ***required*** to file with the FDA "the patent number and the expiration date of any patent which . . . claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1) (2013).[8] The FDA's Orange Book listing rules specify that, among other things, "[f]or patents that claim a method of use, the applicant ***shall submit*** information only on those patents that claim indications or other conditions of use that are described in the pending or approved application." 21 C.F.R. § 314.53(b)(1) (2011) (emphasis added).[9] The FDA has also explained that, "if a method of use is described in the labeling for the drug product, and there is a patent claiming that method of use, the patent ***must be submitted*** for listing in the Orange Book . . . ." *See* Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed, 68 Fed. Reg. 36680 (June 18, 2003) (emphasis added).

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[8] Jazz cites to the 2013 version of the statute because, as explained below, that was the version in place at the time Jazz submitted the '963 patent for listing in the Orange Book. The current version of the statute maintains this requirement. *See* 21 U.S.C. § 355(b)(1)(viii) (2021).

[9] Jazz cites to the version of the regulation in place at the time Jazz submitted the '963 patent for listing. The current version of the regulation maintains this requirement.

Pursuant to the statute and its attendant regulations, Jazz was required to submit the '963 patent for listing in the Orange Book. As set forth above, the package insert for Xyrem® states that "Xyrem is available ***only*** through a restricted distribution program called the XYWAV and XYREM REMS because of the risks of central nervous system depression and abuse and misuse." Ex. B at § 5.3 (emphasis added). Moreover, the FDA only approved Xyrem® on the express condition that the drug would be used according to the "specific restrictions on distribution and use described [in the Xyrem Risk Management Program]." *See* Ex. A at 1; *see also id.* at 2 (describing such restrictions on distribution and use).

The '963 patent claims methods "for treatment of a narcoleptic patient" that comprise the FDA-required conditions of use for Xyrem®, which are described in the Xyrem® REMS. *See supra* at § II(B). Accordingly, the method of using Xyrem® according to its approved REMS is not only a "condition of use" as required by the FDA (*see* 21 C.F.R. § 314.53(b)(1)), but also is "described in the labeling for the drug product" (*see* 68 Fed. Reg. 36680). As such, the '963 patent claims an approved "method of using [the] drug" under both the relevant statute and FDA regulations. *See* 21 U.S.C. § 355(b)(1); 21 C.F.R. § 314.53(b) (requiring listing of "patents that claim indications or other conditions of use"). Thus, far from this being a case of improper listing, Jazz's listing of the '963 patent in the Orange Book was both proper and legally ***required***. If Avadel wishes to have the patent listing statute only strictly allow for method-of-use patents that claim the FDA-approved indications, and not also encompass a "condition of use" for the drug, then the appropriate remedy would be to seek Congressional action to change the statute.

2. Avadel's argument against listing the '963 patent's methods in the Orange Book has already been rejected by the FDA

Avadel argues that, even if the Court were to adopt Jazz's "method" construction, the '963 patent is ineligible for Orange Book listing because it supposedly claims only "a method to safely

distribute" a drug, not "a method of *using*" that drug. D.I. 118 at 9-11. To make this argument, Avadel mischaracterizes Jazz's proposed claim construction. Jazz has not proposed that the '963 patent claims "a method to safely distribute" a drug. Instead, Jazz has proposed that the '963 patent claims methods of using a computer-implemented system to safely distribute GHB for treatment of a narcoleptic patient. Avadel selectively crops Jazz's full construction and the claim itself, both of which explicitly recite "treatment of a narcoleptic patient."

Avadel's cropping is no accident. The FDA recently determined that methods of using a computer-implemented system to safely distribute a drug for treatment of a narcoleptic patient ***are*** methods of using the drug. The FDA made this determination (and rejected the argument Avadel makes here) in the context of deciding that Avadel was required to file a patent certification against the '963 patent. *See generally*, Ex. F.[10] In so doing, the FDA explained that, "although FDA takes a ministerial role in listing patent information in the Orange Book, FDA regularly evaluates whether an applicant's application is consistent with the applicant's assertion that it is not seeking approval for a protected use, as described in a patent use code listed in the Orange Book for the listed drug relied upon." *Id.* at AVDL_01272707.

The FDA's determination is dispositive of Avadel's argument that the '963 patent is ineligible for Orange Book listing if Jazz's construction is adopted. The use code for the

[10] Ex. F is a letter decision of a government agency, which the Court may consider in deciding the instant motion. *See, e.g.*, *Filer v. Polston*, 886 F. Supp. 2d 790, 794 (S.D. Ohio 2012) (explaining that in deciding a motion under Rule 12(c), "a court may consider public records, matters of which a court may take judicial notice, ***and letter decisions of governmental agencies***."); *see also Van Haren v. N.L.R.B.*, No. 01-1667, 2002 WL 1020694, at *1 n.2 (D.N.J. Apr. 15, 2002) ("I may consider 'letter decisions of government agencies' in deciding a Rule 12(b)(6) motion without converting the motion to one for summary judgment."); *Kerrigan v. Chao*, No. 04-1189, 2004 WL 2397396, at *2 (E.D. Pa. Oct. 26, 2004), *aff'd*, 151 F. App'x 129 (3d Cir. 2005) ("a court may consider documents integral to or relied on in the complaint, ***letter decisions of government agencies***, and published reports of administrative bodies, without converting a motion to dismiss into a motion for summary judgment").

'963 patent is U-1110: "METHOD OF TREATING A PATIENT WITH A PRESCRIPTION DRUG *USING* A COMPUTER DATABASE IN A COMPUTER SYSTEM FOR DISTRIBUTION." *See id.* at AVDL_01272699 (emphasis added). [redacted]

FDA's determination is also consistent with the patent listing rules for the Orange Book. When amending those rules in 2015, the FDA reaffirmed that "method of use" in this context is not intended to be limited to using the drug for the treatment of a specific indication in the package insert. Rather, the FDA explained that the "addition of the phrase 'or other conditions of use' . . . reflects that a method-of-use patent that claims a use other than an indication may be submitted for listing in the Orange Book . . . ." Abbreviated New Drug Applications and 505(b)(2) Applications, 80 Fed. Reg. 6830 (February 6, 2015). As such, Avadel's claim that the FDA has, years ago in 2018, "echoed . . . concerns about safety programs like REMS being 'leveraged as a way to forestall [market] entry after lawful IP has lapsed on a brand drug'" (D.I. 118 at 10) rings hollow in light of the FDA's requirement, mere months ago, that Avadel certify against the '963 patent.

For reasons unknown to Jazz, Avadel did not inform the Court of [redacted] in its briefing. Instead, Avadel argues that "Congress addressed" the question presented by its motion and has "made clear that REMS patents were not intended to trigger 30-month stays when it explicitly prohibited REMS patent holders from using such REMS patents to 'block or delay approval of an application' to market a drug product." D.I. 118 at 10 (quoting 21 U.S.C. § 355-1(f)(8)). This is a red herring; the statute that Avadel cites does not prohibit patent owners from asserting REMS patents or the FDA from requiring ANDA or 505(b)(2) NDA filers to submit Paragraph IV certifications when their proposed REMS read on patent use codes. Instead, courts interpreting Section 355-1(f)(8) have held that the import of the statute is that it may impose "antitrust liability . . . where the [REMS] process [not any patent] is manipulated to ***completely preclude*** a generic from ***filing an ANDA***." *In re Suboxone (Buprenorphine Hydrochloride & Naloxone) Antitrust Litig.*, 64 F. Supp. 3d 665, 688 (E.D. Pa. 2014) (emphasis added). Avadel has cited no authority—and Jazz is not aware of any—holding that it is improper under Section 355-1(f)(8) to list a duly issued REMS patent in the Orange Book. Indeed, and as common sense dictates, if Section 355-1(f)(8) did foreclose Orange Book listing and/or patent enforcement, there would have been no reason for Congress to pass another statute in 2021 directing the FDA to solicit public comments on whether REMS patents should ***remain*** eligible for Orange Book listing. *See* Pub. Law 116-290 at § 2(e). Moreover, as the very law review article on which Avadel relies makes clear, Section 355-1(f)(8) would have to be amended (meaning it does not exist in that form today) to preclude a patent owner from enforcing a REMS patent. *See* D.I. 118-1 at 45 (proposing an amendment to Section 355-1(f)(8) to "ensure that [REMS] do not block or delay generic competition").

Accordingly, Avadel's argument that its motion should be granted even if Jazz's "method" construction is adopted was already rejected by the FDA, and Avadel provides no legal basis for a different outcome here.

B. Even if the '963 patent claims computer systems, Jazz was permitted to list it in the Orange Book

Avadel argues that "[r]esolution of claim construction in [its] favor is dispositive of the present motion." D.I. 118 at 6. Not so. Avadel's argument is premised on law that did not (and does not) apply to Jazz's listing of the '963 patent in the Orange Book. Moreover, even if that law were to apply to the '963 patent's Orange Book listing, Avadel's Delisting Counterclaims should still be denied.

1. Avadel relies on the wrong statute and regulations

Citing 21 U.S.C. § 355(b)(1)(A)(viii)(I-II) and 21 C.F.R. § 314.53(b), Avadel argues that the applicable statute "requires that the patents listed [in the Orange Book] claim a 'drug substance,' 'drug product,' or 'a method of using [a] drug.'" D.I. 118 at 7. This is true; such patents—at the time that Jazz submitted the '963 patent for listing in the Orange Book on May 30, 2014[11] and today—were and are required to the be listed in the Orange Book.

Avadel, however, then argues that all other types of patents that are not ***required*** are not "***permitted***[] to be listed in the Orange Book." D.I. 118 at 8 (emphasis added). Citing 21 U.S.C. § 355(c)(2), Avadel argues that "the Hatch-Waxman Act is clear that '[p]atent information that is not the type of patent information required by subsection (b)(1)(A)(viii) *shall not* be submitted" for listing in the Orange Book. *Id.* Avadel ignores, however, that 21 U.S.C. § 355(c)(2) is part of the Orange Book Transparency Act, and that provision was not signed into law until January 5,

[11] *See* Ex. G (Orange Book for Xyrem® with May 2014 submission date for '963 patent).

2021—almost ***seven years after*** Jazz submitted the '963 patent for listing in the Orange Book. ***Before that provision took effect*** (and at the time Jazz submitted the '963 patent for listing in the Orange Book in 2014) the FDA made clear which patents were not permitted for listing in the Orange Book. At that time, the FDA was clear that the only patents that "must not be submitted to FDA" for listing in the Orange Book were: "[p]rocess patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates . . . ." 21 C.F.R. § 314.53(b)(1). Avadel does not and cannot contend that the '963 patent falls within any of these categories.

That leaves a question that Avadel never addresses: Does 21 U.S.C. § 355(c)(2) apply retroactively to the '963 patent? The answer is "no." The Third Circuit has noted the Supreme Court's implementation of a "two-part test" for determining any potential retroactive application of a statute:

> In *Landgraf v. USI Film Products*, the Supreme Court set forth a two-part test for determining whether a particular statute applies retroactively. 511 U.S. at 280, 114 S.Ct. 1483. At the first stage, a court must determine if Congress has expressly prescribed the statute's intended reach. *Id.* If Congress has done so, the inquiry ends, and the court enforces the statute as it is written. *Id.* If the statute is ambiguous or contains no express command, a court must examine whether the statute would have an adverse effect if it were held to be retroactive; that is to say, "whether it would impair rights a party possessed when he acted, increase a party's liability for past conduct, or impose new duties with respect to transactions already completed." *Id.* If the statute would do any of these things, it will not be applied retroactively, "absent clear congressional intent" to the contrary. *Id.*

Lieberman v. Cambridge Partners, L.L.C., 432 F.3d 482, 488-89 (3d Cir. 2005), as amended (Feb. 8, 2006). Attempted retroactive application of 21 U.S.C. § 355(c)(2) fails under both prongs:

First, the "express" language of 21 U.S.C. § 355(c)(2)—in particular, the phrase "shall not be"—unambiguously shows that Congress intended 21 U.S.C. § 355(c)(2) to be applied only prospectively (not retroactively). Courts uniformly agree on this interpretation. *See, e.g.*, *Ghana*

v. Holland, 226 F.3d 175, 182 (3d Cir. 2000) ("[E]very court of appeals to have considered the issue has concluded that the express language of § 1997e(a), which provides that 'no action shall be brought' until the prisoner exhausts administrative remedies, demonstrates Congress's intent that the exhaustion requirement apply only to new actions."); *id.* ("[A] plain reading of the language 'shall be brought' makes clear 'that it applies only to actions that have yet to be brought—not to ones that have already been filed.'" (quoting *Bishop v. Lewis*, 155 F.3d 1094, 1095 (9th Cir. 1998))); *Salahuddin v. Mead*, 174 F.3d 271, 274 (2d Cir. 1999) ("There is no doubt that 'shall' is an imperative, but it is equally clear that it is an imperative that speaks to future conduct. Even the most demanding among us cannot reasonably expect that a person 'shall' do something yesterday."); *Carl Marks & Co., Inc. v. Union of Soviet Socialist Republics*, 665 F. Supp. 323, 337 (S.D.N.Y. 1987) ("The use of 'shall have' indicates prospective application."); *Martropico Compania Naviera S. A. v. Perusahaan Pertambangan Minyak Dan Gas Bumi Negara (Pertamina)*, 428 F. Supp. 1035, 1037 (S.D.N.Y. 1977) ("Indeed, the very wording of section 1330(a) that the 'district courts shall have original jurisdiction' is prospective . . . ."). Because "Congress has expressly prescribed the statute's intended reach . . . , the inquiry ends, and the court enforces the statute as it is written," *Lieberman*, 432 F.3d at 488-89; it does not apply retroactively.

Second, even if the Court were to find that 21 U.S.C. § 355(c)(2) is "ambiguous or contains no express command, [the] court must examine whether the statute would have an adverse effect if it were held to be retroactive; that is to say, whether it would impair rights a party possessed when he acted, increase a party's liability for past conduct, or impose new duties with respect to transactions already completed. If the statute would do any of these things, it will not be applied retroactively, absent clear congressional intent to the contrary." *Lieberman*, 432 at 488-89 (internal quotation marks and citations omitted). Here, there can be no doubt that retroactive

application would have adverse effects upon not only Jazz, but also third parties. For example, retroactive application would mean that Jazz properly listed the '963 patent in the Orange Book on May 30, 2014, had all the statutory rights under the Hatch-Waxman Act through January 5, 2021, but suddenly lost those rights the next day. If that were Congress's intent, it surely would have made that clear. It did not. As another example, retroactive application would impose new duties with respect to both Jazz and a long list of Abbreviated New Drug Application filers who previously certified against the '963 patent in litigation spanning from 2010 until 2018. Again, if Congress intended certification requirements to change for patents listed before enactment of the Orange Book Transparency Act, it surely would have made that clear. Again, it did not. Any one of these is sufficient basis—assuming the Court needs to reach this second prong at all—to conclude that 21 U.S.C. § 355(c)(2) should not be retroactively applied. *Id.*; *see also, e.g.*, *Apotex Inc. v. U.S. Food & Drug Admin.*, 414 F. Supp. 2d 61, 75 (D.D.C. 2006) (explaining that because "retroactive application to situations in which the FDA has already determined which applicant is entitled to exclusivity would disturb settled agency decisions and increase administrative burdens, . . . retroactive applications of the law are not favored in the administrative law context.").

Because 21 U.S.C. § 355(c)(2) is not retroactive, Jazz was permitted to list the '963 patent in the Orange Book under the statute and regulations that were applicable at the time of its listing, and that permissive act has not now been banned. Avadel fails to perform the correct legal analysis. For at least this reason alone, Avadel's reliance on *In re Lantus Direct Purchaser Antitrust Litigation* (D.I. 118 at 8-9), is misplaced. Avadel's reliance on *Lantus* is also misplaced because the patent at issue there ("the '864 patent") claimed "a device intended for use in an injector pen," but it did not claim the injector pen itself, let alone the Lantus SoloSTAR injector pen that was the subject of the NDA; it merely claimed a part used in the SoloSTAR injector. 950

F.3d 1, 8 (1st Cir. 2020). The First Circuit therefore held that, "[u]nder the plain wording of the statute, proper filing of the '864 patent would require not only that it be a patent that claims a drug; it must be a patent that claims the drug (or a method of using the drug) 'for which the applicant submitted' the sNDA." *Id.* (emphases original). The instant case is distinguishable, as the '963 patent specifically recites GHB in a dependent claim, meaning that GHB is encompassed within the claimed prescription drug of the independent claim. *See, e.g.*, D.I. 1, Ex. A at Claims 1, 6. *Lantus* is inapposite for this additional reason.

2. Even if 21 U.S.C. § 355(c)(2) is retroactively applied, Avadel's delisting request should still be denied

Even if the Court were to apply 21 U.S.C. § 355(c)(2) retroactively, Avadel's Delisting Counterclaim should still be denied. Under FDA regulations, Jazz has 30 days to correct any patent listing that is affected by order of a District Court, ***without*** that correction having any impact on Avadel's patent certification. 21 C.F.R. § 314.94(a)(12)(vi)(A)(3). If the Court applies the statute retroactively, Jazz should be permitted the opportunity afforded to it by the FDA's regulations to evaluate any such correction and, if necessary, seek leave to amend its Complaint.

VI. CONCLUSION

For the foregoing reasons, the Court should deny Avadel's partial motion for judgment on the pleadings.

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August 26, 2022

CERTIFICATE OF SERVICE

I hereby certify that on August 26, 2022, 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 August 26, 2022, upon the following in the manner indicated:

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