IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AVADEL CNS PHARMACEUTICALS, LLC
16640 Chesterfield Grove Road, Suite 200
Chesterfield, MO 63005

Plaintiff,

v.

XAVIER BECERRA, Secretary of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201;

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
200 Independence Avenue, SW
Washington, DC 20201;

ROBERT M. CALIFF, Commissioner of Food and Drugs
10903 New Hampshire Avenue
Silver Spring, MD 20993; and

U.S. FOOD AND DRUG ADMINISTRATION
10903 New Hampshire Avenue
Silver Spring, MD 20993,

Defendants.

Case No. 1:22-cv-2159

Filed Under Seal

Oral Argument Requested

MEMORANDUM OF POINTS AND AUTHORITIES
IN SUPPORT OF PLAINTIFF'S MOTION FOR A PRELIMINARY INJUNCTION
OR IN THE ALTERNATIVE SUMMARY JUDGMENT

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES

REGULATIONS

INTRODUCTION

This case is about whether the U.S. Food and Drug Administration ("FDA") can require Plaintiff Avadel CNS Pharmaceuticals, LLC ("Avadel") to file a "patent certification" concerning a third-party's patent that has nothing to do with Avadel's drug, thereby significantly delaying the launch of Avadel's sole product.

Avadel has spent almost a decade developing LUMRYZ, an innovative drug to treat adults with narcolepsy—a rare but debilitating chronic neurological disorder that affects the brain's ability to control sleep-wake cycles. LUMRYZ treats narcolepsy symptoms using sodium oxybate, a central nervous system depressant that helps to induce deep, restful sleep. In contrast to all other FDA-approved gamma-hydroxybutyrate ("oxybate"[1]) products on the market for narcolepsy, which require twice nightly dosing—one dose right before bedtime, and a second dose taken 2.5 to 4 hours later by setting an alarm clock to forcefully awaken the patient in the middle of the night—LUMRYZ utilizes proprietary technology to allow dosing once at bedtime, facilitating a complete night of uninterrupted sleep.

In late 2020, Avadel submitted a new drug application ("NDA") for LUMRYZ pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act ("FDCA"), which provides a streamlined pathway for approval of drugs that are based on the same active ingredient as—but that are not identical to—a previously approved drug. To facilitate notice to owners of previously approved drugs that their intellectual property rights might be impacted by such an NDA, a Section 505(b)(2) applicant must file either a "patent certification" or a "patent statement" regarding certain patents that relate to the previously approved drug and that are listed in an FDA database known as the "Orange Book." Patent certifications are filed when an existing patent

[1] Sodium oxybate is the sodium salt of gamma-hydroxybutyrate.

implicates the new drug, and filing a certification can cause mandatory delays in FDA's approval of the new drug; patent statements, by contrast, are filed when a patent does not implicate the new drug, and cause no approval delays. *See* 21 U.S.C. §§ 355(b)(2)(A), (B).

Jazz Pharmaceuticals plc ("Jazz") is the incumbent manufacturer that produces the only oxybate drugs currently marketed to treat narcolepsy in the United States. Jazz distributes those drugs pursuant to an FDA-mandated Risk Evaluation and Mitigation Strategy ("REMS") to prevent misuse and diversion of sodium oxybate, which has the potential for abuse. Jazz designed its REMS to distribute its drugs through a single, central pharmacy and central database. Jazz also holds a patent pertaining to its single, centralized REMS drug distribution system. LUMRYZ will also be distributed under a REMS, but Avadel has developed its own REMS and will not use Jazz's system. The LUMRYZ NDA properly included a "patent statement" affirming that Jazz's patent pertaining to its REMS system with a single, centralized database is inapplicable.

Rather than approve Avadel's NDA—as FDA was required by statute to have done over 9 months ago—FDA issued a 16-page decision that "constitutes a final decision on the appropriateness of Avadel's" patent statement (the "Patent Decision"). In this Decision, FDA concluded that Jazz's "use code" for its patent—Jazz's description of the scope of its patent that Jazz submitted into FDA's Orange Book—implicates LUMRYZ's NDA. FDA accordingly ordered Avadel to file a patent certification. The result of FDA's Patent Decision is a statutory stay such that, as things now stand, the LUMRYZ NDA cannot be approved until June 2023.

FDA's decision was erroneous for multiple reasons detailed below. FDA's erroneous Patent Decision has caused and will continue to cause Avadel significant and irreparable harm. Avadel's business is solely dependent on the successful commercialization of LUMRYZ, which was anticipated to launch no later than January 2023[redacted]

[redacted]

FDA erred under the Administrative Procedure Act ("APA") in requiring Avadel to submit a patent certification, for four independent reasons, any one of which would require setting aside the Patent Decision. *First*, FDA lacks statutory authority to second-guess an applicant's decision concerning the type of patent certification or statement to submit. Under the plain text of the statute, a certification is required only if, "*in the opinion of the applicant*" a patent "claims a use for such drug for which the applicant is seeking approval," while a patent statement is filed if a patent "does not claim a use for which the applicant is seeking approval under this subsection." 21 U.S.C. § 355(b)(2)(A)-(B) (emphasis added). Congress provided FDA no role in second-guessing the applicant's decision regarding which type of patent certification or statement to file.

Second, even if FDA did have some role in second-guessing applicants' decisions, no certification was required here because Jazz's REMS patent, as described in Jazz's use code, does not claim a use for any drug at all, as required by Section 355(b)(2)(A). Jazz's use code describes a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution." That describes a use of a "computer database," not a use of a drug. It is broadly recognized that REMS patents for distribution systems cannot trigger a patent certification. Nor does Jazz's use code describe a use for sodium oxybate specifically, as required by the statute.

Third, Jazz's use code also cannot trigger a patent certification because Avadel's labeling does not mention any computer database at all. FDA's regulations provide that a drug's proposed

labeling controls whether an applicant must submit a patent certification or statement. 21 C.F.R. § 314.50(i)(1)(iii)(A)–(B). FDA looked beyond the four corners of Avadel's labeling to an extrinsic "LUMRYZ REMS document," to locate a reference to "computer database" and find overlap with Jazz's use code. The Patent Decision therefore violated FDA's own regulation.

Fourth, even if FDA could look beyond the proposed labeling, Jazz's use code requires the use of "a" single, centralized "computer database" for drug distribution, while the proposed LUMRYZ REMS will use four separate and distinct computer databases to control distribution of LUMRYZ. Jazz's use code, describing its patent governing "a" single "database," therefore does not overlap with the proposed LUMRYZ REMS, and FDA erred in concluding otherwise.

For all of these reasons, FDA's Patent Decision ordering Avadel to submit a patent certification regarding Jazz's REMS patent was arbitrary, capricious, and not in accordance with law, in excess of statutory authority, and short of statutory right, and must therefore be set aside. *See* 5 U.S.C. §§ 706(2)(A), (2)(C). But that alone will not remedy Avadel's harms. FDA was required by statute to either approve or set a hearing on the approvability of LUMRYZ by October 15, 2021. Yet, it is now over 278 days later, without such a final approval decision. That is agency action unlawfully withheld under the APA. *See id*. § 706(1). FDA has never suggested that there is any remaining obstacle to approval, apart from its Patent Decision. Just the opposite: FDA expressly told Avadel that its NDA would be subject to approval "immediately," but for its Patent Decision (and the attendant stay on approval that Decision enabled). Defendants should be ordered to issue a final decision on the NDA's approvability within 14 days of this Court's order.

Here, the issues raised by FDA's Patent Decision are legal in nature and Avadel satisfies all the requirements for expedited relief, so Avadel respectfully requests that this motion for a preliminary injunction be adjudicated on an expedited basis in consolidation with the merits. *See*

Fed. R. Civ. P. 65(a)(2). If the Court agrees that Avadel has shown it will succeed on the merits but disagrees that the remaining factors weigh in its favor, Avadel respectfully requests that the Court treat this motion as one for expedited summary judgment.

BACKGROUND

A. Legal Framework for New Drug Applications

The FDCA generally prohibits the sale of a "new drug" unless it has been proven safe and effective. 21 U.S.C. §§ 355(a)-(b). The research and development necessary to secure approval of a new drug generally requires extensive analytical tests, animal studies, and human clinical safety and efficacy trials; takes many years; and is extremely costly. *See id.* § 355(b). Based upon its research and development, a sponsor submits an NDA consisting of, *inter alia*, manufacturing information and all analytical, preclinical, and clinical data. *Id.*

The Hatch-Waxman Amendments of 1984 added more streamlined pathways to NDA approval, including, as relevant to this case, the filing of a Section 505(b)(2) application. *Id.* § 355(b)(2). A Section 505(b)(2) application still requires a massive upfront investment, but the applicant can rely on prior investigations that "were not conducted by or for the applicant" in order to obtain approval of a drug, which can produce savings of time and money in drug development. *Id*. This pathway is typically used for drugs that are based on the same active ingredient as—but which are not identical to—a previously approved drug. *See id.* A Section 505(b)(2) applicant must also file a patent "certification" or a "statement" regarding certain patents pertaining to the previously approved drug that was subject to the prior investigations. *Id.* §§ 355(b)(2)(A)–(B).

Specifically, a Section 505(b)(2) NDA shall include a patent certification, "in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection." *Id.* § 355(b)(2)(A); *see also* 21 C.F.R.

314.50(i)(1)(iii)(B). If a certification is appropriate, the applicant makes one of four certifications: "(i) that such patent information has not been filed [with FDA], (ii) that such patent has expired, (iii) of the date on which such patent will expire, or (iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug . . . ." 21 U.S.C. § 355(b)(2)(A)(i)–(iv).

The statute also provides an alternative pathway for Section 505(b)(2) applicants to identify method-of-use patents that do not fall within certification categories (i) through (iv), *i.e.*, a "patent statement." Specifically, if a "method of use patent" claims a use for the incumbent drug, but "does not claim a use *for which the applicant is seeking approval*," then the applicant must file—in lieu of a patent certification—"a statement that the method of use patent does not claim such a use." *Id.* § 355(b)(2)(B) (emphasis added); *see also* 21 C.F.R. § 314.50(i)(1)(iii)(A).

To evaluate the patents for which a patent certification or statement may be required, FDA instructs the applicant to consult FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, known as the "Orange Book," a database that publishes certain summary information about patents associated with drugs. *See, e.g.*, *Caraco Pharm. Laby's, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405-06 (2012). In addition to patent numbers and expiration dates, the Orange Book contains "use codes" submitted by incumbent patent owners that describe—in the owners' own words—the uses covered by their patents. *Id.*; *see also* 21 C.F.R. §§ 314.53(c)(2)(ii)(P)(3), (e).

Importantly, because FDA admits that it lacks expertise to evaluate patents, FDA does not review the accuracy of Orange Book patent submissions, including use codes, that it receives from patent holders to determine whether they accurately reflect the patented drugs and uses. *See Caraco*, 566 U.S. at 405–06; *Purepac Pharm. Co. v. Thompson*, 238 F. Supp. 2d 191, 196 (D.D.C. 2002), *aff'd*, 354 F.3d 877 (D.C. Cir. 2004). Instead, FDA has assumed a "purely ministerial" role, and "simply lists the patent information that it receives" from incumbent patent holders.

Purepac, 238 F. Supp. 2d at 196. A party wishing to dispute whether an Orange Book use code accurately describes the scope of the underlying patent must first notify FDA and state the basis of its disagreement, and FDA then asks the patent owner to confirm the accuracy of the listing. *Id.* at 196-97. However, unless that owner voluntarily "'withdraws or amends its patent information in response to FDA's request, the agency will not change the patent information'" in the Orange Book in order to render that information accurate. *Id.* (quoting 21 C.F.R. § 314.53(f)).

A certification may affect the date FDA's approval of a new drug takes effect. Generally speaking, if a "paragraph IV" patent certification is filed under 21 U.S.C. § 355(b)(2)(A)(iv) claiming that "such patent is invalid or will not be infringed" by the new drug, FDA's approval will not be made effective for a "thirty-month period," known as the 30 month stay, if the patent owner initiates patent litigation within 45 days of the patent owner's receipt of the applicant's notice of certification. 21 U.S.C. § 355(c)(3)(C). By contrast, there are no statutory delays to the effective date of an NDA approval based on filing patent statements. *See id.* § 355(c)(3).

Absent another limitation on approval (such as the stay referenced above), FDA has a mandatory statutory duty to approve an NDA within 180 days unless one of seven enumerated "grounds for denying approval" is met, such as inadequate tests "to show whether or not such drug is safe for use." 21 U.S.C. § 355(c)(1)(A), (d). Specifically, the statute provides that "[w]ithin one hundred and eighty days after the filing of an application . . . or such additional period as may be agreed upon by the Secretary and the applicant," the Secretary of the Department of Health and Human Services ("HHS"), through FDA, "*shall* either—(A) approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) applies, or (B) give the applicant notice of an opportunity for a hearing before the Secretary . . . on the question whether such application is approvable." *Id.* § 355(c) (emphasis added).

B. The Xyrem and Xywav REMS

Because of the potential for serious side effects and the risk of misuse, oxybate products in the United States must be distributed under a REMS. A REMS "is a risk management plan that uses minimization strategies beyond approved labeling to manage serious risks associated with a drug." *Kyle v. Linden Care, LLC*, No. 19-CV-646-PB, 2020 WL 1853508, at *1 (D.N.H. Apr. 13, 2020). A REMS "can include a Medication Guide or patient package insert, communication plan, one or more elements to assure safe use, [and] an implementation system." *Id.* FDA has discretion to determine whether a REMS is necessary "to ensure that the benefits of the drug outweigh the risks of the drug," by weighing multiple factors, including the "seriousness of any known or potential adverse events." 21 U.S.C. § 355-1(a)(1). If FDA makes such a determination, the applicant must submit a proposed REMS to FDA as part of its NDA. *Id.*

Jazz has always marketed its oxybate products, Xyrem and Xywav, pursuant to a REMS (or, prior to 2007, the predecessor to the REMS regime, a Risk Mitigation Action Plan ("RiskMAP")) that has required a limited distribution system involving a single, central pharmacy that ships the drug directly to patients ("the Jazz REMS" or "Xyrem REMS"). *See In re Xyrem (Sodium Oxybate) Antitrust Litig.*, 555 F. Supp. 3d 829, 840–44 (N.D. Cal. 2021).[2] Notably, Jazz has, for many years, used its REMS and REMS-related patents to maintain its monopoly over sodium oxybate products. *See id.* It is widely acknowledged that "[b]randed drug manufacturers have . . . abused the REMS process to block or delay entry by price-reducing generic competitors." H.R. Rep. No. 116-55, pt. 2, at 4 (2019). For example, in 2010, Jazz sued a competitor that sought to market a generic version of Xyrem for allegedly infringing, among other things, Jazz's REMS-

[2] *See also* Ex. 26 to Divis Decl., *Jazz's Xyrem drug has adverse-events, REMS problems*, Pharm. Com. (Oct. 27, 2011) at 1; Ex. 25 to Divis Decl., Jazz, *The Xywav and Xyrem REMS* at 1, 5.

related patents. *See* Complaint, *Jazz Pharm., Inc. v. Roxane Laby's, Inc.*, No. 10-cv-6108-ES-JAD (D.N.J. filed Nov. 22, 2010), ECF No. 1. The competitor counterclaimed, alleging those patents should not have been listed in the Orange Book and that Jazz was using the patents to improperly "block or delay approval" of generic sodium oxybate drugs.[3] In 2017, FDA criticized the "inconsistent position[s]" Jazz has taken with respect to multiple aspects of its REMS, which "suggest[ed] Jazz's knowledge" that its REMS "could have the effect of preventing . . . competition" for sodium oxybate products.[4] And Jazz is now embroiled in litigation brought by a class of plaintiffs alleging that Jazz has used its REMS to prevent competitors from marketing generic sodium oxybate products. *See In re Xyrem (Sodium Oxybate) Antitrust Litig.*, No. 3:20-md-02966-RS (N.D. Cal.); *see also* Michael A. Carrier & Brenna Sooy, *Five Solutions to the REMS Patent Problem*, 97 B.U. L. Rev. 1661, 1681, 1689, 1704 (2017) (criticizing Jazz's history of abusing its REMS-related patents to delay and prevent the entry of sodium oxybate drugs).

C. Avadel's Development of LUMRYZ

Narcolepsy is a rare but debilitating chronic neurological disorder that affects the brain's ability to control sleep-wake cycles. *See* Declaration of Dr. Bruce Corser ("Corser Decl.") ¶ 4. People suffering from narcolepsy experience excessive daytime sleepiness and may experience uncontrollable episodes in which they fall asleep, even if they are in the middle of an activity like

---

[3] Answer, Affirmative Defenses and Counterclaims to Plaintiff's Complaint ¶ 12, *Jazz Pharm., Inc. v. Roxane Laby's, Inc.*, C.A. No. 10-cv-6108-ES-JAD (D.N.J. filed Dec. 29, 2010), ECF No. 10. That case settled in 2017, and the court did not adjudicate any aspects of the merits of Jazz's claims. *See* Press Release, Jazz Pharm., Jazz Pharmaceuticals Reaches Settlement with Hikma Pharmaceuticals Related to Xyrem Patent Litigation (Apr. 5, 2017), http://investor.jazzpharma.com/news-releases/news-release-details/jazz-pharmaceuticals-reaches-settlement-hikma-pharmaceuticals.

[4] *In re Xyrem*, 555 F. Supp. 3d at 840–44 (quoting Mem. from Trueman Sharp, Deputy Director for the Office of Generic Drugs, FDA, to ANDAs for sodium oxybate oral solution products, *et seq.* at 26 (Jan. 17, 2017)).

driving, working, eating, or talking. *See id.* ¶ 5. It is estimated that fewer than 200,000 Americans suffer from narcolepsy. *Id.*

Although there is no cure for narcolepsy, certain types of medicine can treat some of its symptoms. *Id.* ¶ 6. One such drug is oxybate, a strong central nervous system depressant that helps to induce deep, restful sleep. *Id.*; Ex. 19 to Divis Decl., U.S. National Institute of Health, Sodium Oxybate (Feb. 15, 2021) at 1-2, 7. Since 2002, oxybate has been marketed in the United States exclusively by Jazz under the brand name Xyrem, and, since 2020, Xywav. *See* Corser Decl. ¶ 7; *see also In re Xyrem*, 555 F. Supp. 3d at 840, 877.

A critical problem with all incumbent oxybate products to treat narcolepsy symptoms is that they require two doses, one right before bedtime, and a second dose two-and-a-half to four hours later. Corser Decl. ¶ 8. This necessitates setting an alarm to forcefully awaken the patient in the middle of the night. *See id.*[5] Apart from the obvious disruption to the possibility of an uninterrupted night of continuous, restful sleep—the very goal of treatment—a daily routine of waking in the middle of the night also poses risks to cardiac health, and can be dangerous for narcolepsy patients, who may get up from bed to take the second dose, increasing the risk of nighttime falls and other accidents. *See* Corser Decl. ¶ 9.[6] For instance, a recent study of patients taking Xyrem or Xywav found that 92% of them had gotten out of bed after awakening to take their second dose of sodium oxybate; of those patients, 6% had a fall after awakening to take the second dose. *Id.* ¶ 11; Ex. 2 to Corser Decl., RESTORE Study at 3[redacted]

[5] *See also* Ex. 21 to Divis Decl., Jazz, *Preparing and taking your nightly XYREM doses*, at 2; Ex. 22 to Divis Decl., Jazz, *Learning how to prepare and take XYWAV*, at 2.

[6] [redacted] Ex. 25 to Divis Decl., Jazz, *The Xywav and Xyrem REMS* at 17 ("The sudden onset of sleep . . . has led to falls resulting in injuries, in some cases requiring hospitalization.").

[redacted] Sleep disturbances, like waking up in the middle of the night, are associated with cardiovascular risk. *See* Corser Decl. ¶ 31[redacted] Waking up nightly also reduces patient compliance—patients frequently skip or combine doses—interferes with the sleep of spouses and other bed partners, raises the potential for diversion of the second dose, and forecloses treatment to patients who are unwilling or unable to wake up twice nightly. Corser Decl. ¶¶ 12-19[redacted]

In light of these problems, for almost a decade, Avadel's primary focus has been on the development and FDA approval of LUMRYZ, an innovative sodium oxybate product that uses Avadel's proprietary technology designed to accomplish dosing once at bedtime. Divis Decl. ¶ 6. LUMRYZ allows for dosing once at bedtime, without setting an alarm to wake up in the middle of the night to take a second dose, offering the opportunity for improved sleep and quality of life. Corser Decl. ¶¶ 27-29. Dosing once at bedtime allows for continuous, uninterrupted sleep; reduces the risk of nighttime falls and accidents; and improves patient compliance. *Id.* ¶¶ 30, 32-34[redacted]

D. FDA's Initial Review of the LUMRYZ NDA

On December 15, 2020, Avadel submitted an NDA for LUMRYZ under Section 505(b)(2) of the FDCA. Divis Decl. ¶ 8; Ex. 1 to Divis Decl., Excerpt of LUMRYZ NDA at 1. As part of this NDA application process, Avadel submitted descriptions of its proposed REMS, in compliance with 21 U.S.C. § 355-1. Divis Decl. ¶ 9; *see also, e.g.*, Ex. 2 to Divis Decl., LUMRYZ REMS Document, Module 1.16 (Oct. 14, 2021). Avadel also submitted patent certifications for eight Jazz patents for Xyrem, stating that those patents had expired on June 22, 2020 or would expire on January 4, 2021. Divis Decl. ¶ 11; Exs. 4-5 to Divis Decl., Avadel Patent Certification

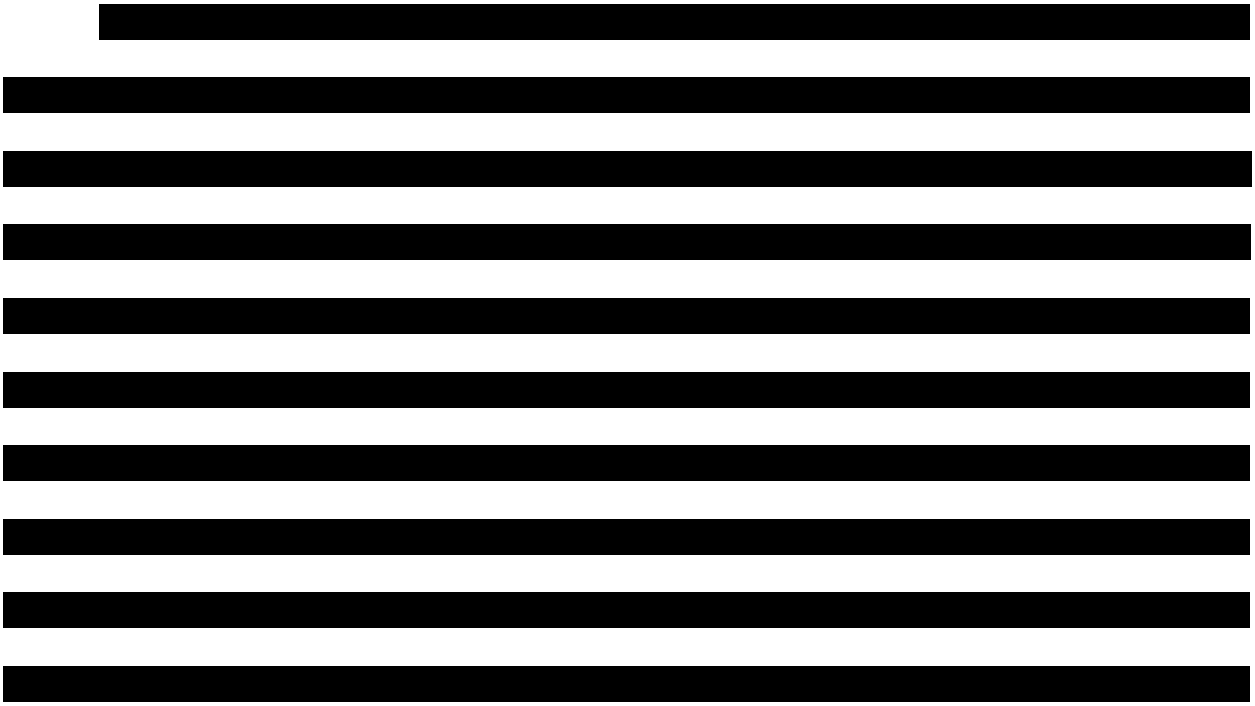
and Statement at 2.[7] Avadel also submitted patent *statements* for six Jazz patents, averring that those patents do not claim a method of using sodium oxybate for which Avadel is seeking approval. *Id.* Those patent certifications and statements are not at issue in this case.

Avadel also submitted a patent statement regarding the Jazz patent connected to the Jazz REMS—U.S. Patent No. 8,731,963 (also known as the '963 patent)—stating that this patent does not cover a method of using sodium oxybate for which Avadel is seeking approval of LUMRYZ. Divis Decl. ¶ 12; Exs. 4-5 to Divis Decl., Patent Certification and Statement at 2-3. For the '963 patent, Jazz submitted a use code, U-1110, into the Orange Book, which describes a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution." Ex. 6 to Divis Decl. In its patent statement, Avadel explained that the '963 patent, as described in U-1110, does not claim any use for sodium oxybate for which Avadel seeks approval because Avadel's proposed LUMRYZ labeling describes no method of treating a patient with the drug using such a computer system. Exs. 4-5 to Divis Decl., Patent Certification and Statement at 2-3. [redacted]

On February 26, 2021, FDA accepted the LUMRYZ NDA for filing, stating that FDA had "completed our filing review, and . . . determined that your application is sufficiently complete to permit a substantive review." Ex. 8 to Divis Decl., FDA, Initial Filing Decision (Feb. 26, 2021)

[7] On December 15, 2020, Avadel submitted to FDA its Patent Certification and Statement. *See* Divis Decl. ¶ 10; Ex. 4 to Divis Decl. On March 25, 2022, Avadel submitted to FDA an updated Patent Certification and Statement, containing materially identical content with respect to the '963 Patent. *See See* Divis Decl. ¶ 10 n.2; Ex. 5 to Divis Decl.

at 1. The NDA was therefore deemed filed as of February 13, 2021 "in accordance with 21 CFR 314.101(a)," *id.*, meaning that FDA's review was required to be complete by August 12, 2021. *See* 21 U.S.C. § 355(c)(1); 21 C.F.R. § 314.101(a)(2). But FDA instead set a "goal date" to complete its review of the LUMRYZ NDA pursuant to the Prescription Drug User Fee Act ("PDUFA") of "October 15, 2021." Ex. 8 to Divis Decl., FDA, Initial Filing Decision at 1. Avadel assented to that extension of FDA's time for review to October 15, 2021. Divis Decl. ¶ 19. Thus, per the FDCA, FDA had until, at the very latest, October 15, 2021, to either approve the LUMRYZ NDA or give Avadel notice of an opportunity for a hearing on whether the NDA is approvable. *See* 21 U.S.C. § 355(c)(1) (requiring FDA action "[w]ithin one hundred and eighty days after the filing of an application under subsection [355](b), *or such additional period as may be agreed upon* by the Secretary and the applicant" (emphasis added)).



[redacted]

E. FDA's Unlawful Refusal to Act on the LUMRYZ NDA

[redacted]

Following the October 15, 2021 PDUFA date, Avadel expeditiously responded to minor additional requests from the Division, including, for example, administrative updates to the carton and container labeling, instructions for use, medication guide, and packaging, and submission of commitment dates for post-marketing non-clinical testing requirements. Divis Decl. ¶ 24. Notably, there is no indication that those minor requests should have or did impact FDA's substantive review of the LUMRYZ NDA, and were of the sort that typically are finalized on the eve of a drug's approval. *Id.* They certainly provide no explanation for FDA's failure to act on the LUMRYZ NDA.

What followed were seven months of inaction during which Avadel repeatedly sought clarity on when FDA's final decision would issue, but FDA declined to provide a revised deadline or explain its failure to act. *Id.* ¶ 25. [redacted]

[redacted]

[redacted]

F. FDA's Patent Decision on Avadel's Patent Statement to the '963 Patent

On May 24, 2022, 221 days after its statutory deadline to render a final decision on the LUMRYZ NDA, either approving the NDA or granting a hearing on the approvability of the NDA, *see* 21 U.S.C. § 355(c)(1), FDA finally informed Avadel of its decision on only one aspect of the NDA. Divis Decl. ¶ 30. FDA found that "Avadel is seeking approval of a condition of use that is claimed by the '963 patent, as described by the U-1110 use code, and thus Avadel's proposed section 505(b)(2)(B) statement to address this patent is inappropriate." Ex. 15 to Divis Decl. at 2, 10. FDA ordered Avadel to "provide an appropriate patent certification under 21 CFR 314.50(i)(1)(i) to address the '963 patent," *i.e.*, a paragraph IV certification. *Id.* at 16.

In its Patent Decision, FDA evaluated whether the LUMRYZ NDA seeks "approval for the protected use described in the U-1110 use code." *Id.* at 11. To determine the "use" for which the LUMRYZ NDA sought approval, FDA looked not only to the LUMRYZ "prescribing

information," *i.e.*, the information provided to physicians concerning how to use the drug, but also at a separate "Lumryz REMS document," because the prescribing information purportedly did not "provide the complete description of all the Lumryz REMS program requirements." *Id.* at 11-12. The "Lumryz REMS document," FDA explained, describes that "Avadel must establish and maintain 'validated, secure, separate, and distinct databases of all REMS participants enrolled, certified and/or disenrolled in the REMS Program, including a patient database, certified prescriber database, certified pharmacy database, and disenrolled prescriber database.'" *Id.* at 12 (quoting Ex. 2 to Divis Decl., LUMRYZ REMS Document (Module 1.16) (Oct. 14, 2021) at 7).

FDA compared this "Lumryz REMS document" to the "face" of the U-1110 code, which describes the use of "*a* computer database." *Id.* (citation omitted). Rather than applying an ordinary English meaning, FDA "interpret[ed] 'a' computer database" as used in U-1110 "to refer to any—one or more—computer databases." *Id.* Based on this capacious reading of U-1110, FDA therefore found that the LUMRYZ REMS document's reference to "multiple computer databases" qualified as use of "a computer database" within the scope of U-1110. *Id.* Accordingly, FDA concluded that Avadel's Section 505(b)(2)(B) patent statement, which stated that the LUMRYZ labeling did "not contain any reference to use of a computer database," was "inappropriate," and ordered Avadel to "provide an appropriate patent certification under 21 CFR 314.50(i)(1)(i) to address the '963 patent" described in U-1110. *Id.* at 16. FDA explained that its Patent Decision "constitutes a final decision" that Avadel must submit a certification to the '963 patent. *Id.* at 1.

On June 6, 2022, Avadel filed a paragraph IV patent certification as FDA had ordered it to do, but did so under protest, emphasizing that Avadel maintained that its initial patent statement regarding the '963 patent was proper, and that Avadel believed that FDA's determination that it could not approve LUMRYZ without a certification to that patent was erroneous. Divis Decl. ¶ 36;

Ex. 16 to Divis Decl., Revised Patent Certification and Statement (June 6, 2022) at 2. Avadel explained it would withdraw its certification should the Patent Decision be set aside. *Id.*

The '963 patent does not expire until December 17, 2022, and Jazz has asserted (and FDA has acknowledged) that Jazz is entitled to an additional six months of "pediatric exclusivity" with respect to the '963 patent under 21 U.S.C. § 355a(b)(1)(B)(i)(II), until June 17, 2023.[9] Accordingly, FDA's Patent Decision meant that the LUMRYZ NDA could not be approved immediately, at the soonest by July 22, 2022 (within 45 days of Avadel's patent certification submissions), and potentially not until June 17, 2023, if Jazz were to sue Avadel for alleged infringement on the '963 patent as a result of FDA's mandated certification. *See* 21 U.S.C. § 355(c)(3)(C).

G. FDA's Tentative Approval and Jazz's Lawsuit

Six weeks after Avadel filed its patent certification to the '963 patent under protest, on July 18, 2022, FDA issued a tentative approval of the LUMRYZ NDA, finding that the LUMRYZ NDA is "tentatively approved under 21 CFR 314.105 for use as recommended in the agreed-upon enclosed labeling . . . and submitted labeling." Divis Decl. ¶ 37; Ex. 35 to Divis Decl. (Tentative Approval) at 1. As explained by FDA, a tentative approval is not a final or effective approval of an NDA, and does not permit a drug to come to market. *Id.* at 2; 21 C.F.R. § 314.105(a) ("A drug product that is granted tentative approval is not an approved drug . . . ."). Rather, a tentative approval provides that an NDA is approvable, provided that a future contingency is met, such that the NDA would be entitled to final, effective approval at a later time. 21 C.F.R. § 314.105(a) ("FDA will issue a tentative approval letter . . . if a 505(b)(2) application otherwise meets the

[9] *See* Ex. 6 to Divis Decl., U-1110 at 1 ("PED[IATRIC]" "patent expire date" "06/17/2023"); Ex. 37 to Divis Decl., New Pediatric Labeling Information Database – Detail, Xyrem at 1 (similar).

requirements for approval under the [FDCA], but cannot be approved . . . because there is a period of pediatric exclusivity for the listed drug . . . ."); *Mylan Labs., Inc. v. Thompson*, 449, 389 F.3d 1272, 1281 (D.C. Cir. 2004) (noting "tentative approval" issued pending patent "expiration date").

FDA's Tentative Approval stated that the "listed drug(s) upon which your application relies is subject to a period of patent protection and your application contains a certification(s) to one or more patents under section 505(b)(2)(A)(iv) of the FD&C Act." Ex. 35 to Divis Decl. at 1. The Tentative Approval further explained that, consistent with FDA's prior communications with Avadel in June 2022 and 21 U.S.C. § 355(c)(3)(C), the final approval of the LUMRYZ NDA would be "made effective immediately, unless an action is brought for infringement of one or more of the patents that were the subject of a paragraph IV certification." Ex. 35 to Divis Decl. at 2; *see also* 21 U.S.C. § 355(c)(3)(C) ("the approval shall be made effective immediately unless, before the expiration of 45 days after the date on which the notice described in subsection (b)(3) is received, an action is brought for infringement of the patent that is the subject of the certification . . ."). FDA further explained that "[i]f such a patent infringement action is brought prior to the expiration of 45 days . . . your application would be subject to a 30-month stay of approval . . . ." Ex. 35 to Divis Decl. at 2; *see also* 21 U.S.C. § 355(c)(3)(C) ("If such an action is brought before the expiration of such [45] days, the approval may be made effective upon the expiration of the thirty-month [stay]," subject to certain qualifications and exceptions.).

On July 15, 2022, Jazz filed a lawsuit against Avadel for alleged infringement of the '963 patent in the United States District Court for the District of Delaware, in case number 1:22-cv-00941-UNA. Divis Decl. ¶ 41; *see also* Ex. 36 to Divis Decl., Jazz Complaint. Due to FDA's Patent Decision and the resultant patent certification to the '963 patent under protest, this lawsuit triggered the stay identified by FDA. *See* 21 U.S.C. § 355(c)(3)(C). That stay now precludes

approval of the LUMRYZ NDA until expiration of the '963 patent term and the related term of pediatric exclusivity in June 2023 (unless the stay is terminated earlier by, for example, delisting of the '963 patent from the Orange Book).[10] By contrast, were FDA's Patent Decision to be vacated, there would be no remaining obstacle to "immediate[]" final approval of the LUMRYZ NDA. Ex. 35 to Divis Decl. at 2.

On July 21, 2022, Avadel filed the Complaint in this matter, along with the instant motion for preliminary injunction or, in the alternative, summary judgment, to remedy FDA's violation of the FDCA through its Patent Decision.

ARGUMENT

All factors favoring immediate relief are met here. Avadel has shown (1) a likelihood of success on the merits; (2) a likelihood of irreparable harm in the absence of preliminary relief; (3) a balance of equities in its favor; and (4) that the proposed injunction would further the public interest. *See League of Women Voters of U.S. v. Newby*, 838 F.3d 1, 6 (D.C. Cir. 2016). The issues presented by this Motion are legal in nature, and Avadel therefore requests consolidation of preliminary relief with the merits. *See* Fed. R. Civ. P. 65(a)(2). In the alternative, if the Court agrees with Avadel on the merits but disagrees that the equitable factors weigh in Avadel's favor, Avadel respectfully requests that the Court enter expedited summary judgment.

For all of these reasons and those detailed below, the Court should set aside the Patent Decision and order Defendants to issue a final decision on the LUMRYZ NDA within 14 days of this Court's decision.

[10] *See* Ex. 6 to Divis Decl., U-1110 at 1 ("PED[IATRIC]" "patent expire date" "06/17/2023"); Ex. 37 to Divis Decl. at 1 (similar); *see also* 21 U.S.C. §§ 355a(c)(1)(B)(i), (ii) (providing for extended pediatric exclusivity, barring competitor entry).

I. AVADEL WILL SUCCEED ON THE MERITS OF ITS CHALLENGE TO THE PATENT DECISION

A court "shall . . . hold unlawful and set aside agency action . . . found to be . . . arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," or "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right." 5 U.S.C. §§ 706(2)(A), (2)(C); *see also* 5 U.S.C. § 702. FDA's Patent Decision is all of those.

A. FDA Lacks Authority To Evaluate the Propriety of Section 505(b)(2) Applicants' Decisions To Submit Patent Certifications or Statements

Either a patent certification *or* statement must be included in any Section 505(b)(2) NDA. *See* 21 U.S.C. § 355(b)(2)(A)–(B); *Genus Lifesciences, Inc. v. Azar*, No. 1:20-CV-00211 (TNM), 2021 WL 270409, at *3 (D.D.C. Jan. 27, 2021). But FDA lacks statutory authority to second-guess an NDA applicant's decision *which* of these to file, a certification or statement, much less to compel an NDA applicant to alter its chosen submission (here, a patent statement), to a different submission (a patent certification). Instead, the statute unambiguously places the decision concerning which type of certification or statement to make solely with the applicant.

Section 355 does not provide for *any* FDA involvement in evaluating the appropriateness of patent certifications and statements. 21 U.S.C. § 355. Indeed, far from statutory silence, Section 355(b)(2)(A) expressly provides that an applicant "shall" submit "a certification, *in the opinion of the applicant and to the best of his knowledge*, with respect to each patent which claims the drug . . . which claims a use for such drug for which the applicant is seeking approval under this subsection . . . ." *Id.* § 355(b)(2)(A) (emphasis added). By contrast, Section 355 contains other provisions that grant FDA express decision-making authority over other aspects of the NDA process. *See, e.g.*, *id.* § 355(c)(4) (FDA is to "make[] a determination that a full scale production facility is necessary to ensure the safety or effectiveness of the drug"); *id.* § 355(i)(1) (providing

"discretion of the Secretary" to promulgate rules). FDA's regulations note the decisive role of the applicant: Orange Book submissions must contain "adequate information to assist 505(b)(2) . . . *applicants in determining* whether a listed method-of-use patent claims a use for which the . . . applicant is not seeking approval." 21 C.F.R. § 314.53(c)(2)(ii)(P)(3) (emphasis added)).

Contrary to the governing statute, FDA has taken the position in a Federal Register preamble that FDA possesses authority to compare Orange Book patent use codes with NDA applications, and to overrule the NDA applicant's determination as to whether the use code and the "use for such drug for which the applicant is seeking approval" in the NDA overlap, 21 U.S.C. § 355(b)(2)(A), such that a certification is required. Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36676, 36,682–83 (June 18, 2003). But, having declined to codify its purported interpretation in a binding regulation, FDA's assertion of authority is "not entitled to any special consideration" by this Court in deciding whether FDA actually possesses such authority, *Perry v. Novartis Pharma. Corp*., 456 F. Supp. 2d 678, 684 (E.D. Pa. 2006); *see also* 21 C.F.R. § 10.85(d)(1).[11] As discussed, it does not possess such authority.

In asserting this authority, FDA acknowledged "the absence of explicit statutory language" allowing it to second-guess an applicant's determination, but nonetheless concluded its position "is most consistent with the general balance adopted in Hatch-Waxman." 68 Fed. Reg. at 36,682–83. FDA also speculated that if Section 505(b)(2) applicants "could always avoid the possibility of a 30-month stay" by submitting a patent statement without FDA's approval, "there would be

[11] And, of course, even if it had codified its interpretation, an agency regulation cannot be applied when it conflicts with the statute. *See, e.g.*, *United Airlines, Inc. v. Transp. Sec. Admin.*, 20 F.4th 57, 63 n.3 (D.C. Cir. 2021) ("To the extent that the . . . regulation . . . may conflict with the statute, 'the statute clearly controls.'" (quoting *Murphy v. IRS*, 493 F.3d 170, 176 (D.C. Cir. 2007))).

little reason for any applicant to submit a paragraph IV certification for a method-of-use patent," thereby "essentially eliminat[ing] the certification, notice, and litigation process." *Id.*

FDA frequently tries to "find" authorization for its extra-statutory regulatory innovations in Congress's alleged silence, and courts just as frequently rebuke those attempts. *See*, *e.g., Eagle Pharm., Inc. v. Azar*, 952 F.3d 323, 331 (D.C. Cir. 2020) (finding that the FDCA's "plain language" foreclosed FDA's interpretation, and rejecting FDA's claim that an FDCA "provision is ambiguous because it is silent"); *Catalyst Pharm., Inc. v. Becerra*, 14 F.4th 1299, 1312 (11th Cir. 2021) ("FDA's interpretation . . . is contrary to the clear statutory language"). An agency cannot delegate to itself authority that Congress did not authorize by statute, based on policy considerations. *Id.* Worse, here Congress was not silent at all. Using unique terminology not found elsewhere in the FDCA, Congress assigned this role to the applicant, not FDA, by providing that a certification is filed based on "the opinion of the applicant and to the best of his knowledge." 21 U.S.C. § 355(b)(2)(A). FDA's interpretation that FDA may overrule the applicant's opinion renders Congress's chosen language surplusage. *See Obduskey v. McCarthy & Holthus LLP*, 139 S. Ct. 1029, 1037 (2019) (courts "presum[e] that statutes do not contain surplusage").

Congress's express deference to the "opinion of the applicant" with respect to whether to submit a patent certification also makes good sense. The purpose of the Hatch-Waxman Amendments was to "speed the introduction" of drugs to market. *Caraco*, 566 U.S. at 405. And FDA's concerns that there would be "little reason for any applicant to submit a paragraph IV certification" absent FDA policing is not well-founded. 68 Fed. Reg. at 36,682. It is highly unlikely that applicants will knowingly and intentionally falsify patent submissions to the government, contrary to the statute; intentional fraud on FDA is unlawful. *See, e.g.*, 18 U.S.C. § 1001(a). While deferring to the "opinion of the applicant" might result in fewer certifications

and more statements in close cases where the patent issues are reasonably debatable, that is a decision for Congress to make, and it was hardly irrational for Congress to defer to the "opinion of the applicant," rather than FDA, given Congress's goal of expediting entry, and FDA's admitted lack of "expertise" and "authority" to engage in patent law analysis. 68 Fed. Reg. at 36,683.

Indeed, it is on the basis of that same professed lack of "expertise" that FDA has assumed a "purely ministerial" role in accepting all "patent submissions" in the Orange Book, regardless of whether they accurately reflect the scope of the underlying patent, because FDA "[l]ack[s] the resources or the expertise to determine the validity or scope of patent claims." *Purepac*, 238 F. Supp. 2d at 196; *see also* Ex. 15 to Divis Decl., Patent Decision at 9 n.34 ("FDA has not evaluated . . . whether the use code published in the Orange Book accurately reflects what is covered by the '963 patent"). Thus, FDA's rules "do not actually keep non-conforming patents, submitted in violation of the rules, out of the Orange Book." *Purepac*, 238 F. Supp. 2d at 208. And if FDA lacks the authority or competence to determine whether the scope of the underlying patent matches with an Orange Book use code, how could it engage in the more complex exercise of evaluating the scope of the use code (reflecting the purported patent scope), and determining whether that scope overlaps with the NDA itself? Avadel respectfully submits that the question answers itself.

In sum, FDA does not possess statutory authority to second-guess NDA applicants' patent statements and to compel them to file patent certifications in their place. FDA's decision to do so in this case was therefore contrary to law. Because Avadel was entitled to determine itself whether, "in the opinion of the applicant," the patent described in U-1110 "claims a use for such drug for which the applicant is seeking approval," FDA's decision ordering Avadel to submit a patent certification in place of its statement as to Jazz's patent described in U-1110 must be set aside.

B. FDA's Decision To Compel A Patent Certification Was Erroneous Because U-1110 Does Not Describe A Method Of Using A Drug, Much Less Sodium Oxybate

Even assuming that FDA were authorized to second-guess the type of patent statement or certification submitted by Section 505(b)(2) applicants, FDA's Patent Decision ordering Avadel to submit a patent certification was arbitrary, capricious, and contrary to law, because the use code U-1110 does not describe the use of *any* drug at all, and certainly not the use of *the drug* for which Avadel seeks approval—*i.e.*, sodium oxybate.

By way of background, FDA has found that it must make its "overlap" determination as to whether an incumbent patent "claims a use for such drug" for which the applicant seeks approval, 21 U.S.C. § 355(b)(2)(A), solely with reference to the Orange-Book listed "use code," not the actual patent itself—which, as described above, FDA has disclaimed sufficient competency to interpret. *Supra* at 23. Specifically, "FDA will not approve" a Section 505(b)(2) application if the new entrant's proposed "label overlaps at all with the brand's use code," and "FDA takes that code as a given: It does not independently assess the patent's scope or otherwise look behind the [use code] description." *Caraco*, 566 U.S. at 406 (citing 68 Fed. Reg. at 36,682-83); *see also Purepac*, 238 F. Supp. 2d at 205 (noting FDA's "deference to NDA holders' characterizations of the scope of use patents" in the Orange Book). Thus, the Patent Decision found that FDA was constrained to review only the use code U-1110, and not the actual '963 patent, in evaluating whether that patent claims a use for sodium oxybate for which Avadel seeks approval. Ex. 15 to Divis Decl., Patent Decision at 9 & n.34 ("FDA relies on the use code provided by Jazz and listed for Xyrem in the Orange Book," and "FDA has not evaluated what the '963 patent actually covers or whether the use code . . . accurately reflects what is covered by the '963 patent.").

The Court might reasonably wonder how FDA's exclusive reliance on a "use code" as the basis for this comparative exercise, and refusal to consider the underlying '963 patent, is consistent with the statute, given that an applicant must submit a certification "with respect to *each patent* . . . which claims a use for such drug for which the applicant is seeking approval under this subsection *and for which information is required to be filed under paragraph (1) or subsection (c)*." 21 U.S.C. § 355(b)(2)(A) (emphases added). That is, the statute bases the relevant comparative exercise on whether an incumbent "patent" in fact "claims a use" for which the applicant seeks approval. *Id.* And the statute relegates the role of an "Orange Book" "use code" to a subsidiary clause, referring to information required to be filed under "paragraph (1) or subsection (c)," *i.e.*, the provisions requiring submission of certain information into the "Orange Book," 21 U.S.C. §§ 355(b)(1)(A)(viii) and 21 U.S.C. §§ 355(c)(2). Nor does a "use code" fully suffice to describe what the "patent" "claims": FDA has acknowledged that its "use codes" were limited to "240 total characters" due to "limitations of our database system," and thus "240 characters may not fully describe the use as claimed in the patent." 68 Fed. Reg. at 36,683.[12]

That is an interesting issue, but it can be left for another day. Here, the Court need not decide whether FDA's sole reliance on a "use code" is permissible, because even under FDA's "use code" regime, Avadel prevails.[13] Under that regime, certifications must be filed only with respect to a "use code" that contains a description of a patent "which claims *the drug*" or "claims a use for *such drug*" for which the applicant seeks approval. 21 U.S.C. § 355(b)(2)(A) (emphases

[12] Today, a "use code" may extend to 250 characters. *See* FDA, Final Rule, Abbreviated New Drug Applications and 505(b)(2) Applications, 81 Fed. Reg. 69,580, 69,598 (2016).

[13] To be clear, Avadel would prevail under either FDA's existing "use code" regime or under an evaluation of the underlying "patent" itself, for the reasons detailed below. *See infra* at 25-36.

added); *see also supra* at 5-6. Here, neither of those conditions are met, because the use code U-1110 does not describe a use of *any* drug at all, and certainly not a use of sodium oxybate.

1. U-1110 does not describe any drug or a use for any drug

The '963 patent, as described in U-1110, does not claim any "drug" or a use for any "drug," which are threshold requirements for patent certifications under 21 U.S.C. § 355(b)(2)(A).

A certification is required only for a patent that "claims the *drug*" or "claims a use for such *drug* for which the applicant is seeking approval under this subsection." 21 U.S.C. § 355(b)(2)(A) (emphases added). But U-1110 does not describe a "use" for any "drug;" it describes a "method of treating a patient with a prescription drug *using a computer database in a computer system for distribution*." Ex. 6 to Divis Decl., U-1110 at 1 (emphasis added); *cf.* Ex. 7 to Divis Decl., '963 Patent at 25-27, Claims 1-28 (same). On its face, the "use" described in U-1110 is not a use of a drug, but a "us[e]" of a "computer database" for "distribution." Ex. 6 to Divis Decl., U-1110 at 1.

In accordance with the statutory text, commentators have observed that REMS drug distribution patents should not trigger patent certifications under 21 U.S.C. § 355(b)(2)(A) because "REMS patents . . . do not claim 'the drug' or 'a method of using' the drug . . . ." Carrier & Sooy, *supra* at 1672 (emphasis in original); *see also* Comment of Mylan N.V. at 2, No. FDA-2020-N-1127, *Listing of Patent Information in the Orange Book; Establishment of a Public Docket; Request for Comments* (Aug. 31, 2020) (arguing that REMS patents "do not 'claim' the relevant drug or a method of using such drug," and that there is a "well-documented history of brand sponsors' misuse of the REMS requirements for anticompetitive purposes"). FDA itself raised questions in 2020 as to whether "REMS-related patents" are in fact "the type of patents that must be submitted" to the Orange Book, but over two years later, FDA has not reached any decision on

that matter. *See* Listing of Patent Information in the Orange Book; Request for Comments, 85 Fed. Reg. 33,169 (June 1, 2020); *see also* Ex. 15 to Divis Decl., Patent Decision at 9-10 & n.34.

Statutory context confirms that REMS patents do not claim a "use" for any "drug" that could trigger a patent certification requirement. *First*, a REMS is not a "use" for which an applicant "seek[s] approval" "*under this subsection*," *i.e.*, under 21 U.S.C. § 355(b), as is required to trigger a patent certification. 21 U.S.C. § 355(b)(2)(A). Instead, a REMS is a set of restrictions imposed by FDA under a distinct section altogether, 21 U.S.C. § 355-1. Thus, Avadel could not "seek[] approval under this subsection" of any REMS that could potentially overlap with U-1110. 21 U.S.C. § 355(b)(2)(A). *Second*, in 2007, when Congress first enacted Section 355-1 to create the REMS framework, Congress expressly provided that "[n]o holder of an approved covered application shall use any element to assure safe use required by the Secretary under this subsection to block or delay approval of an application under section 505(b)(2)." Food and Drug Administration Amendments Act of 2007, Pub. L. No. 110-85, 121 Stat. 823, 932 (codified at 21 U.S.C. § 355-1(f)(8)). That is, Congress provided that REMS distribution restrictions required under Section 355-1, like the Jazz REMS, shall not "block or delay approval" of a Section 505(b)(2) NDA. *Id.* Yet that is precisely what FDA and Jazz are doing here. *Third*, REMS patents should not be Orange Book listed in the first place (and could not trigger a certification) because a REMS patent does not "claim[] the drug for which the applicant submitted the application" or "claim[] a method of using such drug for which approval is sought or has been granted . . . ." 21 U.S.C. § 355(b)(1)(A)(viii). Congress was aware of the abusive practice of incumbents submitting improper patent information into the Orange Book, and in 2020, Congress amended Section 355 to confirm that patents that do not claim "the drug" or a "method of using such drug" are barred from the Orange Book: "Patent information that is not the type of patent information required by

subsection (b)(1)(A)(viii) shall not be submitted." Orange Book Transparency Act of 2020, Pub. L. No. 116-290, 134 Stat. 4889, 4890 (2021) (codified at 21 U.S.C. § 355(c)(2)).

FDA may argue that the Court should ignore the statute's requirement that a certification be filed only when a patent "claims a use for such drug for which the applicant is seeking approval under this subsection," 21 U.S.C. § 355(b)(2)(A), and instead apply FDA's regulation at 21 C.F.R. 314.50(i)(1)(iii)(B), which requires certification to an Orange Book use code describing a patent that claims a "condition of use" that is included in the NDA:

> If the labeling of the drug product for which the applicant is seeking approval includes an indication or other condition of use that, according to the patent information submitted under section 505(b) or (c) of the Federal Food, Drug, and Cosmetic Act [in the Orange Book] and § 314.53 or in the opinion of the applicant, is claimed by a method-of-use patent, the applicant must submit an applicable certification under paragraph (i)(1)(i) of this section.

21 C.F.R. § 314.50(i)(1)(iii)(B). Indeed, the Patent Decision found "Avadel is seeking approval of a condition of use that is claimed by the '963 patent." Ex. 15 to Divis Decl. at 10.

But FDA would be wrong in arguing that a patent certification could be required by its regulation when it is plainly not required by the statute. If 21 C.F.R. § 314.50(i)(1)(iii)(B) were to be read to expand patent certifications beyond what Section 355(b) requires, it would conflict with the statute and therefore could not be applied. *See United Airlines*, 20 F.4th at 63 n.3.

And even applying this regulation, U-1110 does not describe a patent that claims a "condition of use" for sodium oxybate, as required by 21 C.F.R. § 314.50(i)(1)(iii)(B). FDA has previously explained to this Court that its "longstanding" and "consistent view" is that a "condition of use" is strictly limited to "how, to whom, and for which purposes the drug is *administered*." Ex. 24 to Divis Decl., FDA, Motion to Dismiss or for Summary Judgment at 19–20, 21, *ViroPharma, Inc. v. Hamburg*, No. 1:12-cv-00584-ESH (D.D.C. Sept. 4, 2012), ECF No. 53 (emphasis added). As FDA told this Court, "'[c]onditions of use' thus include a drug product's

indications[14] and dosing regimen," but "do not include all contents of a drug product's labeling." *Id.* at 19-20. Thus, FDA explained that a change from an "approved condition of use" would therefore "have to change how, to whom, or for which purposes a drug is administered." *Id.* at 27. FDA's "consistent" interpretation of a "condition of use" also makes good sense as a matter of plain English: A drug is "used" by administering it to a patient; a drug is not "used" by distributing it. *See* Use, Merriam Webster (2022) ("consume," "take," or "put into . . . service"). A "condition of use" or restriction of "use" thus restricts how the drug is administered, not how it is distributed.

Accordingly, a REMS *distribution* patent like the one described in U-1110 does not describe "how, to whom, or for which purposes a drug is administered," and thus does not claim a "condition of use" for a drug (*see* Ex. 24 to Divis Decl., FDA, Motion at 27, *ViroPharma*,), as would be required to trigger a patent certification under 21 C.F.R. 314.50(i)(1)(iii)(B). [redacted] No certification was required.

2. U-1110 does not describe a method of using sodium oxybate

Nor does U-1110 describe a patent that "claims the *drug*" or "claims a use for *such drug* for which the applicant is seeking approval under this subsection." 21 U.S.C. § 355(b)(2)(A) (emphases added). Instead, U-1110 describes a "method of treating a patient with *a prescription drug* using a computer database in a computer system for distribution." Ex. 6 to Divis Decl., U-1110 at 1 (emphasis added). FDA therefore erred in determining that Avadel was required to submit a Section 355(b)(2)(A) certification for any patent described by U-1110.

[14] An "indication" is "[a] general description of the disease or condition the device will diagnose, treat, prevent, cure, or mitigate…." 21 C.F.R. § 814.20(b)(3)(i).

It is well established in analogous circumstances that to "claim" a drug or a method of using that drug under Section 355 of the FDCA, a patent must expressly describe that drug. For example, in *United Food & Commercial Workers Local 1776 & Participating Employers Health & Welfare Fund v. Takeda Pharmaceutical Co. Ltd.*, the Second Circuit analyzed the "claims the drug" and "claims a method of using such drug" language in Section 355(b)(1) of the FDCA, and found that where an incumbent "patent claim . . . fails to explicitly include the drug," *i.e.* the relevant "active ingredient," it neither claims the drug nor a method of using the drug for purposes of Section 355(b)(1). 11 F.4th 118, 134 (2d Cir. 2021). Similarly, in *In re Lantus Direct Purchaser Antitrust Litigation*, the First Circuit found that a patent was improperly Orange-Book listed because it claimed only a "mechanism [ ] intended for use in a 'drug delivery device'" yet failed to specifically "mention the drug" for which an NDA was submitted, and thus, the patent did not "claim the drug" or "a method of using the drug" under Section 355(b). 950 F.3d 1, 3, 6, 8 (1st Cir. 2020); *see also Hoechst-Roussel Pharm., Inc. v. Lehman*, 109 F.3d 756, 759 (Fed. Cir. 1997). Accordingly, FDA cannot compel Avadel to submit a certification to the patent described in U-1110, because U-1110 does not describe a use of sodium oxybate at all.

C. FDA Violated Its Own Regulations By Referring To Materials Beyond The LUMRYZ Labeling In Concluding That U-1110 Claims A Use Of Sodium Oxybate For Which Avadel Seeks Approval.

Avadel was not required to submit a patent certification, for the additional reason that there is no overlap between the LUMRYZ labeling and U-1110's description of the '963 patent.

FDA has bound itself by regulation to look only to a NDA's proposed "labeling" in determining the new use for which an NDA seeks approval, and thus, whether a patent certification is required. Specifically, a patent "certification"—not a statement—must be filed when "the *labeling* of the drug product for which the applicant is seeking approval includes an indication or

other condition of use that, according to the [Orange Book] is claimed by a method-of-use patent. . . . ." 21 C.F.R. § 314.50(i)(1)(iii)(B) (emphasis added); *see also id.* § 314.50(i)(1)(iii)(A) (a patent "statement" must be filed when "the *labeling* for the drug product for which the applicant is seeking approval does not include an indication or other condition of use that is covered by the [incumbent's] method-of-use patent." (emphasis added)); 81 Fed. Reg. at 69,640, 69,598 (similar). FDA therefore cannot look beyond the NDA's proposed "labeling" in determining the scope of the drug use for which the NDA seeks approval. *See Nat'l Env't Dev. Ass'n's Clean Air Project v. EPA*, 752 F.3d 999, 1009 (D.C. Cir. 2014) ("an agency is bound by its own regulations").

Here, the LUMRYZ labeling makes no reference to a database or computer system, and therefore cannot overlap with U-1110, which describes a "method of . . . using a computer database in a computer system for distribution." *Compare* Ex. 15 to Divis Decl. at 18-27 *and* Ex. 35 to Divis Decl. at 19-40 (LUMRYZ labeling), *with* Ex. 6 to Divis Decl., U-1110 at 1. FDA effectively admitted as much, when it explained that it needed to look beyond the draft LUMRYZ label and "prescribing information" to find any database or computer system. Ex. 15 to Divis Decl., Patent Decision at 11-12. "FDA agree[d] that the LUMRYZ prescribing information" in the LUMRYZ label "does not explicitly mention the use of a computer database." *Id.* at 14. But FDA found that the LUMRYZ prescribing information "does not provide the complete description of all the LUMRYZ REMS program requirements," and in an unprecedented move in the "unique circumstance" in which both the LUMRYZ and Xyrem "prescribing information do[] not provide the complete description of all the . . . REMS program requirements," FDA "also considered the proposed LUMRYZ REMS document." *Id.* at 11-12. And FDA found that this "LUMRYZ REMS document"—not LUMRYZ's label—"describes the use of multiple computer databases" for "distribution of the drug product" to patients, and thus overlaps with U-1110. *Id.*

But the LUMRYZ REMS document on which FDA's Patent Decision turned is not part of the LUMRYZ "labeling," as required by 21 C.F.R. 314.50(i)(1)(iii)(A)-(B). The FDCA provides two distinct, separate pathways for FDA's review and approval of an NDA's "labeling" and a proposed "REMS," respectively. *Compare* 21 U.S.C. §§ 355(b)(1)(A)(vi), (c)-(d) (labeling review) *with* 21 U.S.C. §§ 355-1(a)(1), (h) (REMS review). Moreover, a drug's labeling consists of only "labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article." 21 U.S.C. § 321(m). But the "LUMRYZ REMS document" FDA relied on will neither be included in the LUMRYZ label or upon the drug or its container or wrappers, or accompanying the drug. *See* Ex. 15 to Divis Decl., Patent Decision at 11-12; Divis Decl. ¶ 32. Indeed, FDA has admitted on multiple occasions that a REMS and REMS documentation generally are not part of the "labeling" of a drug. Instead, a REMS "is a risk management plan that uses minimization strategies *beyond approved labeling* to manage serious risks associated with a drug."[15] Courts have concurred with FDA's view that a REMS "allows for additional FDA restrictions beyond those set forth on the drug's labeling." *Am. Coll. of Obstetricians & Gynecologists v. FDA*, 472 F. Supp. 3d 183, 190 (D. Md. 2020).[16] Indeed, in the instant Tentative Approval, FDA repeatedly distinguished between the LUMRYZ "labeling" and "Content of Labeling" and the LUMRYZ "REMS." Ex. 35 to Divis Decl. at 2, 3, 18, 21.

---

[15] Ex. 27 to Divis Decl., Questions and Answers: FDA Approves a Class Risk Evaluation and Mitigation Strategy (REMS) for Transmucosal Immediate-Release Fentanyl (TIRF) Medicines ("Q&A"), FDA (Dec. 28, 2020), https://www.fda.gov/drugs/information-drug-class/questions-and-answers-fda-approves-class-risk-evaluation-and-mitigation-strategy-rems-transmucosal.); Ex. 28 to Divis Decl., *Questions and Answers on the iPLEDGE REMS*, FDA (last visited June 5, 2022), https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-ipledge-rems.

[16] FDA might point to instances in the record in which Avadel suggested that a REMS might form part of a product's labeling in certain circumstances. But those statements are inapplicable here, and in any event, could not excuse the FDA's failure to comply with its own regulations.

Given this lack of overlap between the proposed LUMRYZ labeling and U-1110's description of the '963 patent, no patent certification was required under FDA's regulation. For instance, in *Hospira, Inc. v. Burwell*, the court explained that, in the analogous ANDA context of generic drugs, FDA can lawfully approve drug applications including only patent statements "for broad, general indications even though they may partially overlap with a protected method of use," if "all express references to the protected use [are] omitted from the labeling." No. GJH-14-02662, 2014 WL 4406901, at *17 (D. Md. Sept. 5, 2014) ("the law requires a focus only on the *label*"); *see also H. Lundbeck A/S v. Lupin Ltd*., No. CV 18-88-LPS, 2021 WL 4944963, at *106 (D. Del. Sept. 30, 2021) (insufficient evidence of patent infringement where label omitted references to protected use (collecting cases)). Absent any overlap between the proposed LUMRYZ labelling and U-1110's description of the '963 patent, no certification was required under 21 C.F.R. 314.50(i)(1)(iii)(B), and the Patent Decision erred in concluding otherwise.

D. U-1110 Does Not Describe A Use Of Sodium Oxybate For Which Avadel Seeks Approval In The LUMRYZ NDA.

Even if the "LUMRYZ REMS document" did form part of LUMRYZ's "labeling," there is no overlap between that document and U-1110's description of the '963 patent.

Specifically, the LUMRYZ REMS document does not contain any reference to any "method of treating a patient with a prescription drug using *a computer database in a computer system* for distribution," as described in in U-1110.[17] That is because the LUMRYZ REMS document describes the use of four distinct databases that will be maintained and queried to ensure appropriate distribution of LUMRYZ through the distinct LUMRYZ REMS, while the Jazz REMS

[17] *Compare* Ex. 2 to Divis Decl., LUMRYZ REMS Document at 1-10, *with* Ex. 6 to Divis Decl., U-1110 at 1; *cf.* Ex. 7 to Divis Decl., '963 Patent at 1-30.

patent described by U-1110 covers only the use of "*a*" single computer database in "*a*" single, centralized "computer system" for distribution.

Jazz's description in use code U-1110 of "using a computer database in a computer system for distribution" is unambiguous: It clearly refers to the use a single computer database in a single computer system to accomplish drug distribution. As the Supreme Court recognized last year, the article "a," as in "a notice," refers to a "single" item, like "'a' single document," as a "singular article." *Niz-Chavez v. Garland*, 141 S. Ct. 1474, 1480 (2021). Thus, a statutory requirement to provide "a notice" refers to a single document and cannot refer to "two documents." *Id.* Indeed, the very use of the "article 'a'" provides evidence that the drafter is referring to "a discrete, countable thing," specifically, a "single" thing, as the "ordinary meaning" of "a." *Id.* at 1480-81.

The description of the '963 patent in U-1110 as using "a" singular "computer database" and "a" singular "computer system," rather than multiple "computer databases" and "systems," was not an accident: The '963 patent claims the use of *one* "central database," "a single computer database" used for "[a] drug distribution system and method [that] utilizes a *central pharmacy and database* to track all prescriptions." Ex. 7 to Divis Decl., '963 patent at 22, col. 1 line 48–50; *id.* at 28, col. 8 line 42–43 (emphasis added). [redacted]

Simply put, U-1110, like the '963 patent, does not claim the use of multiple databases for drug distribution as described in the LUMRYZ REMS document. Nor can FDA rewrite Jazz's description of its patent in U-1110 today, to describe any prescription drug distribution system that uses one *or more* databases. Not only would that be an unreasonable construction of U-1110, but if Jazz's description of its purported patent were to sweep so widely, it would purport to capture essentially any "prescription drug" "distribution" system using any number of "database[s]" (alteration added), of pharmacies, hospitals, and other healthcare providers nationwide.

Finally, even if FDA's construction of "a computer database in a computer system for distribution" to refer to any number of computer databases could be a permissible construction in some circumstances, it is not in this case, because the Patent Decision's reasoning is internally contradictory. On the one hand, FDA adopted a capacious view of "a computer database" as any number of computer databases because "on its face" U-1110 does not "limit the description of the protected method of use to a single computer database in a computer system for distribution." Ex. 15 to Divis Decl., Patent Decision at 15. That is, "[o]n its face, the use code does not mention a 'central database' or a 'central pharmacy'; instead, the use code mentions 'a computer database.'" *Id.* FDA so reasoned because, "[c]onsistent with its ministerial role, FDA has not evaluated what the '963 patent actually covers or whether the use code published in the Orange Book accurately reflects what is covered by the '963 patent." *Id.* at 9 n.34. But in the very same Decision, FDA found that, in order to "determine what is described by the '963 patent as reflected in the U-1110 use code," FDA needed to "expand its review of the use code beyond the [Xyrem] prescribing information to also consider the Xyrem REMS document." *Id.* at 10-11. And that "Xyrem REMS document" in turn "describes . . . a 'validated, secure database,' known as the Central Database, containing information for 'all REMS participants . . . .'" *Id.* at 11. Accordingly, FDA concluded

that this "Xyrem REMS document" that details the use of a single "Central Database" "describes the protected method of use claimed by the U-1110 use code." *Id.*

In sum: FDA reasoned that it could not look beyond the "face" of the U-1110 "use code" to find in favor of Avadel, *i.e.*, to agree that the '963 patent was so narrowly limited to a single, central database such that Avadel could avoid a patent certification requirement; but that FDA could look beyond the "use code" to "determine what is described by the '963 patent," *i.e.*, the use a single "Central Database," solely for purposes of sweeping Avadel into a patent certification requirement in the first place. *Id.* at 9-12. But if FDA decides to look to materials extrinsic to the "use code" at all, it must do so consistently. *See, e.g.*, *Transactive Corp. v. United States*, 91 F.3d 232, 237 (D.C. Cir. 1996) ("agency action is arbitrary when the agency offer[s] insufficient reasons for treating similar situations differently"); *Purepac*, 354 F.3d at 884 (agency's internally "inconsistent" reasoning is arbitrary and capricious). As this Court explained in *Purepac*, "FDA cannot profess allegiance to the [applicant's] descriptions of its patents only to disregard unambiguous patent descriptions submitted by that company because it finds them inconsistent with the agency's contrived construction" of the patent-holder's own submissions. 238 F. Supp. 2d at 209. FDA's Patent Decision must be set aside.

II. ALL EQUITABLE FACTORS SUPPORT IMMEDIATE RELIEF

The relevant equitable considerations—irreparable harm, the balance of equities, and the public interest, *see League of Women Voters*, 838 F.3d at 6—all favor immediate relief.

A. Avadel Will Suffer Irreparable Harm Absent Immediate Relief

[redacted]

[redacted]

The fact that the movant "has little hope of obtaining 'adequate compensatory or other corrective relief at a later date' if the injunction does not issue . . . weighs heavily in favor of granting the injunction." *O'Donnell Constr. Co. v. District of Columbia*, 963 F.2d 420, 428 (D.C. Cir. 1992). Here, Avadel cannot be compensated by the government for its losses caused by delayed market entry, because FDA has sovereign immunity. *See, e.g.*, *Nalco Co. v. EPA*, 786 F. Supp. 2d 177, 188 (D.D.C. 2011) ("Where a plaintiff 'cannot recover damages from the defendant due to the defendant's sovereign immunity . . . any loss of income . . . is irreparable *per se*.'"). And even if there were a defendant from whom damages could be recovered, Avadel's losses are difficult to calculate with reasonable certainty, which also makes them irreparable. *See* Divis Decl. ¶ 48; *O'Donnell Constr. Co*., 963 F.2d at 428 ("inherently speculative showing" of "how much profit [defendant] would have made" demonstrates irreparable harm); *Bell Helicopter Textron, Inc. v. Airbus Helicopters*, 78 F. Supp. 3d 253, 274-75 (D.D.C. 2015) ("risk of future reputational harm, lost sales, and lost customers" found irreparable where such losses "defy attempts at valuation").

LUMRYZ is Avadel's sole product candidate. Divis Decl. ¶ 45. Avadel has no other prospective revenue streams. *Id.* [redacted]

[redacted]

[redacted] Avadel's competitor, Jazz, will maintain its monopoly over current or prospective patients who otherwise could choose LUMRYZ, precluding Avadel from obtaining any cost recovery of its substantial investments in developing LUMRYZ. *See id.* ¶¶ 64-68. [redacted]

[redacted]

[redacted]

[redacted]

The harm to narcolepsy patients nationwide from FDA's Decision is also irreparable. *See Int'l Long Term Care, Inc. v. Shalala*, 947 F. Supp. 15, 18 (D.D.C. 1996) (finding HHS decision caused "irreparable and unnecessary harm" to plaintiff's patients); *Ass'n of Cmty. Cancer Ctrs. v. Azar*, 509 F. Supp. 3d 482, 500 (D. Md. 2020). Avadel's research and the opinion of numerous physicians demonstrate significant health and quality-of-life benefits from once-at-bedtime LUMRYZ. *Supra* at 10-11; Corser Decl. ¶¶ 20-25, 35. Yet FDA's unlawful decision ensures months of delay in LUMRYZ coming to market [redacted]

B. The Balance Of Equities And Public Interest Favor Immediate Relief.

The balance of equities and public interest also weigh in Avadel's favor. These two factors merge "when the Government is the opposing party." *Nken v. Holder*, 556 U.S. 418, 435 (2009). As detailed above, FDA's decision will inflict serious harm on narcolepsy patients

nationwide, who will remain unwilling or unable to use existing, burdensome oxybate treatments, or will be faced with the serious compliance challenges, diminished quality of life, and health and safety risks associated with incumbent twice-nightly sodium oxybate products. *Supra* at 10-11. FDA will not suffer any injury from being required to abide by its statutory mandate. The only party that could conceivably be harmed is Jazz from increased competition; but permitting Jazz to unlawfully perpetuate its monopoly over all oxybate treatments is not in the public interest. *See, e.g.*, *Otsuka Pharm. Co., Ltd. v. Torrent Pharm. Ltd., Inc*., 99 F. Supp. 3d 461, 507 (D.N.J. 2015) (extending incumbent drug manufacturer's "protection from competition" "would result in a disservice to the public interest," which benefits from "increased competition"). And "[t]here is generally no public interest in the perpetuation of unlawful agency action." *League of Women Voters*, 838 F.3d at 12. "To the contrary, there is a substantial public interest 'in having governmental agencies abide by the federal laws that govern their existence and operations.'" *Id.*

III. DEFENDANTS SHOULD BE ORDERED TO COMPLY WITH THEIR STATUTORY DUTY TO FULLY ADJUDICATE THE LUMRYZ NDA WITHIN FOURTEEN DAYS OF THIS COURT'S ORDER

For the reasons set forth above, the Court should "hold unlawful and set aside" the Patent Decision. 5 U.S.C. § 706(2). That alone, however, will not fully remedy Avadel's harms. FDA had a mandatory statutory duty to either approve the LUMRYZ NDA or offer an opportunity for a hearing on the approvability of the NDA by October 15, 2021. *See* 21 U.S.C. § 355(c)(1). FDA is now 278 days past that deadline. FDA kept Avadel's NDA in regulatory limbo for over seven months beyond its October deadline, even as FDA indicated that its scientific review was substantively complete. *Supra* at 12-13. FDA's Tentative Approval now confirms that, apart from the REMS patent certification, there are no scientific issues remaining outstanding. Ex. 35 to Divis

Decl. at 1-3. The Court should "compel agency action unlawfully withheld," 5 U.S.C. § 706(1) and require Defendants to issue a final decision adjudicating the NDA within 14 days.

The Court may enter an order compelling an agency to act when it has failed to make a "decision by a statutory deadline." *Sandoz Inc. v. Leavitt*, 427 F. Supp. 2d 29, 34 (D.D.C. 2006) (quoting *Norton v. S. Utah Wilderness All.*, 542 U.S. 55, 63 (2004)). Under the FDCA, when FDA receives a Section 505(b)(2) NDA, FDA "shall" make one of two decisions after 180 days "or such additional period as may be agreed upon by the Secretary and the applicant" has passed: (1) approve the application if no grounds for denial apply, or (2) offer the applicant a hearing to address whether the NDA is approvable. 21 U.S.C. § 355(c)(1). The 180-day (or mutually agreed-upon) deadline is not advisory: It is binding and judicially enforceable, as this Court has previously held in compelling FDA to adjudicate an NDA by that deadline. *Sandoz*, 427 F. Supp. 2d at 38.

Here, FDA admitted that it received the LUMRYZ NDA on December 15, 2020. Ex. 8 to Divis Decl., FDA, Initial Filing Decision (Feb. 26, 2021) at 1. Then, on February 26, 2021, FDA found that the LUMRYZ NDA was "sufficiently complete to permit a substantive review." *Id.* The application was deemed filed on February 13, 2021, 60 days after December 15, 2020. *See id.*; 21 C.F.R. § 314.101(a). FDA's review was required to be complete within 180 days, by August 12, 2021. 21 U.S.C. § 355(c)(1). But FDA set a PDUFA "user fee goal date" for the LUMRYZ NDA of "October 15, 2021," and Avadel assented to that extension. Divis Decl. ¶ 19; Ex. 8 to Divis Decl., FDA, Initial Filing Decision (Feb. 26, 2021) at 1. Therefore, the "agreed" October 15, 2021 deadline became both binding and mandatory. 21 U.S.C. § 355(c).

Yet now, more than 278 days later, there is *still* no final decision either approving the NDA, or granting a hearing on the approvability of the NDA. That is "agency action unlawfully withheld." 5 U.S.C. § 706(1). Given FDA's lengthy inaction—and now the delay caused by its

Patent Decision [redacted]. Avadel respectfully requests that the Court order FDA to issue a final decision adjudicating the NDA within 14 days of the Court's order.

Because FDA has violated a clear statutory deadline, relief from this Court should follow. *See Am. Forest Res. Council v. Nedd*, No. CV 15-01419 (RJL), 2021 WL 6692032, at *2 (D.D.C. Nov. 19, 2021) ("The imperative nature of [Section 706(1)] not only empowers, but *requires*, courts to issue orders mandating agency action when it is unlawfully withheld." (emphasis in original)); *South Carolina v. United States*, 907 F.3d 742, 756 (4th Cir. 2018) (if a party has "demonstrated an unlawfully withheld agency action under § 706(1), the court must enter an appropriate order and secure the agency's compliance with the law" irrespective "of equitable . . . considerations").

But even were this Court to apply equitable considerations, it should reach the same result. Some courts have applied the so-called "*TRAC*" factors when deciding whether to grant equitable relief based on claims of agency delay. *See Telecomm. Rsch. & Action Ctr. v. FCC* ("*TRAC*"), 750 F.2d 70, 80 (D.C. Cir. 1984). Those factors include: "a rule of reason[ ]," whether "Congress has provided a timetable," that "delays . . . are less tolerable when human health and welfare are at stake," "the effect of expediting delayed action on agency activities of a higher or competing priority," "the interests prejudiced by delay," and that no "impropriety" by the agency is required to find "agency action is unreasonably delayed." *Id.* Here, all of these factors favor an order requiring immediate action. A "rule of reason" favors immediate action, because Avadel is not attempting to "jump the line" in front of earlier-in-time NDA applicants, but to end FDA's disparate treatment of the LUMRYZ NDA. *Id.* Throughout the past several months, FDA has

approved other orphan-drug-designated drugs similar to LUMRYZ on or before PDUFA dates.[18] More generally, a cursory review of FDA's NDA approval website reveals hundreds of NDAs that FDA has approved or acted upon in the last six months,[19] all while the LUMRYZ NDA has "languished," *Sandoz*, 427 F. Supp. 2d at 39. Accordingly, there is no basis to conclude that "expediting delayed action" would improperly impact "agency activities of a higher or competing priority." *TRAC*, 750 F.2d at 80. Instead, it is clear that FDA is able to fulfill its statutory duties to review and decide NDAs. *See Sandoz*, 427 F. Supp. 2d at 38. Congress has provided an express, 180-day "timetable" for action, the breach of which also favors immediate action. *TRAC*, 750 F.2d at 80. Further inaction is also contrary to the "health and welfare" of tens of thousands of narcolepsy patients, and Avadel's own "interests" will also continue to be "prejudiced" with each passing day in which Avadel lacks market access. *Id.*; *supra* at 37-39. As identified in *TRAC* and *Sandoz*, the Court need not find any "impropriety" in Defendants' inaction to order compliance with the law. 750 F.2d at 80; 427 F. Supp. 2d at 39. The Court should compel immediate action.

---

[18] As an example, on February 28, 2022, FDA approved two drugs on the same day as their PDUFA dates: an NDA received by FDA on March 30, 2021, for CTI BioPharma's VONJO (pacritinib) for the treatment of myelofibrosis with severe thrombocytopenia; and an NDA received by FDA on March 31, 2021, for Janssen/Legend Biotech's CARVYKTI (ciltacabtagene autoleucel) for the treatment of adults with relapsed and/or refractory multiple myeloma. *See* Ex. 29 to Divis Decl., Letter from FDA, to CTI BioPharma Corp (Feb. 28, 2022) (on file at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/208712Orig1s000ltr.pdf); Ex. 30 to Divis Decl., *FDA approves drug for adults with rare form of bone marrow disorder*, FDA (Mar. 1, 2022), https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-drug-adults-rare-form-bone-marrow-disorder; Ex. 31 to Divis Decl., Letter from FDA, to Janssen Biotech, Inc. (Feb. 28, 2022) (on file at a https://www.fda.gov/media/156572/download); *CARVYKTI* (Feb. 28, 2022), https://www.fda.gov/vaccines-blood-biologics/carvykti.

[19] *Drugs@FDA: FDA-Approved Drugs*, FDA, https://www.accessdata.fda.gov/scripts/cder/daf/ (allowing search of "Drug Approval Reports by Month").

CONCLUSION

For the foregoing reasons, this Court should grant Avadel's motion for a preliminary injunction or, in the alternative, summary judgment; set aside FDA's Patent Decision ordering Avadel to submit a patent certification; and order FDA to take final action on the LUMRYZ NDA within 14 days of the Court's order.

Respectfully submitted,

Dated: July 21, 2022

/s Philip J. Perry

Philip J. Perry (DC Bar No. 434278)
Andrew D. Prins (DC Bar No. 998490)
John R. Manthei (DC Bar No. 447123)
Nicholas L. Schlossman (DC Bar No. 1029362)

LATHAM & WATKINS LLP
555 Eleventh Street NW, Suite 1000
Washington, DC 20004
Tel: (202) 637-2200
Fax: (202) 637-2201
Email: philip.perry@lw.com
andrew.prins@lw.com
john.manthei@lw.com
nicholas.schlossman@lw.com

Attorneys for Plaintiff