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

REDACTED

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff Avadel CNS Pharmaceuticals, LLC ("Avadel") brings this suit against Defendants Xavier Becerra, in his official capacity as Secretary of Health and Human Services; the U.S. Department of Health and Human Services ("HHS"); Robert Califf, in his official capacity as Commissioner of Food and Drugs; and the U.S. Food and Drug Administration ("FDA"), and alleges as follows:

PRELIMINARY STATEMENT

1. Narcolepsy is a rare but serious chronic neurological disorder that affects the brain's ability to control sleep-wake cycles. People suffering from narcolepsy experience excessive daytime sleepiness and may experience uncontrollable episodes of falling asleep during the daytime. It is estimated that less than 200,000 Americans suffer from narcolepsy.

2. Although there is no cure for narcolepsy, certain types of medicine can treat some of its symptoms. One such drug is gamma-hydroxybutryate ("oxybate"), a central nervous system depressant that helps to induce deep, restful sleep.

3. Since 2002, oxybate has been marketed in the United States exclusively by Jazz Pharmaceuticals plc ("Jazz") under the brand name Xyrem, and, since 2020, Xywav. But a critical problem with Jazz's oxybate products is that they are immediate release formulations requiring two doses—one right before bedtime, and a second dose between two-and-a-half to four hours later—which necessitates people already suffering from a sleep disorder to set an alarm to forcefully awaken in the middle of the night to take the second dose.

4. Avadel is a biopharmaceutical company focused on researching and developing drugs to treat narcolepsy. For almost a decade, Avadel's focus has been on the development of LUMRYZ™, an innovative product that uses proprietary technology designed to enable dosing once before bedtime of sodium oxybate (a type of oxybate). That once before bedtime dosing regimen allows for improved patient safety, compliance, and quality of life by enabling patients to avoid setting an alarm to awaken in the middle of the night to take a second dose, thus offering the possibility of an uninterrupted night of restorative sleep.

5. To provide these benefits to patients, on December 15, 2020 Avadel submitted a new drug application ("NDA") for LUMRYZ to the U.S. Food and Drug Administration ("FDA" or the "Agency") pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act

("FDCA"), which provides streamlined pathways for approval of drugs that are based on the same active ingredient as—but which are not identical to—a previously approved drug.

6. 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 a "patent certification" or a "patent statement" regarding certain patents that relate to the previously approved drug. 21 U.S.C. §§ 355(b)(2)(A), (b)(2)(B).

7. Patent certifications are filed when an existing patent 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. FDA instructs applicants to make this determination by reviewing FDA's "Orange Book," an FDA database that publishes certain summary information about patents associated with approved drugs.

8. With its NDA, Avadel submitted to FDA required information about potential overlap between the LUMRYZ NDA and patents held by Jazz. Jazz distributes Xyrem and Xywav pursuant to an FDA-mandated Risk Evaluation and Mitigation Strategy ("REMS"), which was designed by Jazz such that distribution occurs through a single, centralized pharmacy and database, to prevent misuse and diversion of oxybate—which has potential for abuse. Jazz also holds a patent that it alleges pertains to its single, centralized REMS drug distribution database, U.S. Patent No. 8,731,963 (the "Jazz REMS patent" or "'963 patent"), which it has filed under "use code" U-1110 in FDA's Orange Book.

9. LUMRYZ will also be distributed under a REMS, but Avadel has developed its own REMS system and will not use Jazz's. The LUMRYZ NDA accordingly included a "patent statement" affirming that the Jazz REMS patent, as described by Jazz's use code U-1110, does not

"claim[ ] a use for such drug for which the applicant is seeking approval," because Jazz's description of that patent in its use code U-1110 does not overlap with the LUMRYZ NDA. *See* 21 U.S.C. § 355(b)(2)(A).

10. 525 days after Avadel filed its NDA—and 221 days after FDA was required by law to render its final decision on the NDA—FDA instead rendered a final decision on only one discrete subcomponent of the LUMRYZ NDA, Avadel's patent statement to the '963 patent.

11. In a 16-page decision that "constitutes a final decision on the appropriateness of Avadel's section 505(b)(2)(B) [patent] statement" (the "Patent Decision"), FDA concluded that Jazz's use code U-1110 *does* describe a patent that "claims a use for such drug for which the applicant is seeking approval" through the LUMRYZ NDA, and ordered Avadel to "provide an appropriate patent certification under 21 CFR 314.50(i)(1)(i)" certifying to an overlap between the Jazz REMS patent, as described in Jazz's use code, and the LUMRYZ NDA.

12. FDA reasoned that because Jazz's use code describes the use of "a computer database in a computer system for distribution," and because the proposed LUMRYZ REMS will use four computer databases for distribution, Avadel must submit a patent certification certifying to the alleged overlap between the two.

13. The Jazz REMS patent does not expire until December 17, 2022, and Jazz has asserted 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. 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 relevant patent certification submissions), and potentially not until June 17, 2023, if Jazz were to sue Avadel for alleged infringement on the Jazz REMS patent as a result of FDA's mandated certification. *See* 21 U.S.C. § 355(c)(3)(C).

14. In response to FDA's Patent Decision, Avadel filed the FDA-ordered "patent certification" under protest on June 6, 2022, explaining its continued disagreement with FDA's decision that Jazz's use code describes a patent that "claims a use for such drug for which the applicant is seeking approval." *Id.* § 355(b)(2)(A).

15. On July 18, 2022, FDA issued a tentative approval of the LUMRYZ NDA (the "Tentative Approval"). A tentative approval is not a full, final, or effective approval of an NDA. Rather, a tentative approval provides that an NDA is approvable, provided that a future contingency is met that would permit the NDA to obtain final approval at a later time.

16. FDA's Tentative Approval explained that 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" by July 22, 2022. FDA further clarified 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 . . . ."

17. 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, case number 1:22-cv-00941-UNA. 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.

18. That stay now precludes the immediate approval of the LUMRYZ NDA, as would have otherwise been possible in July 2022, 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).

19. FDA's erroneous Patent Decision—coupled with Jazz's lawsuit—has caused and will continue to cause Avadel significant and irreparable harm. Avadel's business is solely

dependent on the successful commercialization of LUMRYZ[redacted]

21. 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 FDA's Patent Decision.

22. As an initial matter, under the plain statutory text, FDA lacks authority to second-guess an NDA applicant's decision concerning the type of patent certification or statement to submit.

23. In addition, even if FDA did have some role in second-guessing applicants' decisions to submit patent statements or certifications, no certification was warranted here because Jazz's description of the Jazz REMS patent in its use code U-1110 does not claim a "use" for *any* "drug," much less a use for sodium oxybate, as required by 21 U.S.C. § 355(b)(2)(A).

24. Next, the patent description in Jazz's use code, describing a computerized system for drug distribution, does not "claim[ ] a use for such drug for which the applicant is seeking approval," *id.*, for the additional reason that Avadel's labeling does not mention any computer system at all, as required by 21 C.F.R. § 314.50(i)(1)(iii)(A)-(B).

25. And finally, even if FDA could look beyond Avadel's proposed labeling, Jazz's use code still does not "claim[ ] a use for such drug for which the applicant is seeking approval," 21

U.S.C. § 355(b)(2)(A), because the LUMRYZ REMS calls for the use of four separate and distinct computer databases for distribution of LUMRYZ, rather than the single, centralized computer system described by Jazz's use code.

26. For all of these reasons, FDA's Patent Decision ordering Avadel to submit a patent certification to the '963 patent was arbitrary, capricious, contrary to law, in excess of statutory jurisdiction and authority, and short of statutory right, and must therefore be set aside. *See* 5 U.S.C. § 706.

27. But that alone will not remedy Avadel's harms. FDA was required by statute to either finally approve or set a hearing on the approvability of LUMRYZ within 180 days after the filing date, or a later time agreed to between FDA and Avadel—in this case, October 15, 2021.

28. Yet, more than 580 days have passed since the LUMRYZ NDA was filed, and it is now over 278 days past FDA's October 15, 2021 statutory deadline to render its final approval decision on the NDA. That is agency action unlawfully withheld under the APA. *See* 5 U.S.C. § 706(1). FDA has never suggested that there is any remaining obstacle to NDA approval, apart from this patent certification. Just the opposite: FDA expressly told Avadel that its NDA would be subject to approval "immediately," but for its Patent Certification decision (in combination with the lawsuit filed by Jazz as a result of the Patent Certification decision).

29. In light of Defendants' ongoing violation of law and unlawful refusal to act on this NDA as required by the FDCA, Defendants should be ordered to take final action on the LUMRYZ NDA within 14 days of the Court's order.

30. Here, the issues raised by FDA's Patent Decision are legal in nature and Avadel satisfies all the requirement for expedited relief. Avadel respectfully requests preliminary injunctive relief adjudicated on an expedited basis in consolidation with the merits.

PARTIES

31. Avadel is the owner of NDA No. 214755 for LUMRYZ. Avadel is a Delaware limited liability company with its principal United States place of business at 16640 Chesterfield Grove Road, Suite 200, Chesterfield, MO 63005.

32. Xavier Becerra is the Secretary of Health and Human Services and the head of HHS. In this official capacity, Secretary Becerra has ultimate responsibility for activities at HHS, including the actions complained of herein. He conducts his governmental activities at 200 Independence Avenue, S.W., Washington, D.C. 20201. His governmental activities also occur nationwide.

33. HHS is a department of the United States. Its headquarters and principal place of business are at 200 Independence Avenue, S.W., Washington, D.C. 20201. Its governmental activities occur nationwide.

34. Robert Califf is the Commissioner of Food and Drugs and the head of FDA. His governmental activities occur nationwide.

35. FDA is an agency of the United States and a division of HHS. FDA's headquarters and principal place of business are at 10903 New Hampshire Avenue, Silver Spring, MD 20903. Its governmental activities occur nationwide.

JURISDICTION, VENUE, EXHAUSTION, AND FINAL AGENCY ACTION

36. This Court has jurisdiction pursuant to 28 U.S.C. § 1331. This action arises under the Administrative Procedure Act ("APA"), 5 U.S.C. §§ 701-06. Avadel's prayers for a declaratory judgment and injunctive relief are authorized by the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; the APA, 5 U.S.C. §§ 701-06; and 28 U.S.C. § 1361.

37. Venue is proper in this District under 28 U.S.C. § 1391(e) because at least one Defendant is an officer or agency of the United States and resides in this District.

38. FDA explained in its Patent Decision that its Decision "constitutes a final decision on the appropriateness of Avadel's section 505(b)(2)(B) [patent] statement" submitted as part of the LUMRYZ NDA. The Patent Decision is a final agency action reviewable under the APA. *See* 5 U.S.C. §§ 551, 704, 706; *Purepac Pharm. Co. v. Thompson*, 238 F. Supp. 2d 191, 202–03 (D.D.C. 2002), *aff'd*, 354 F.3d 877 (D.C. Cir. 2004).

39. FDA's failure to approve LUMRYZ within the statutorily mandated timeline for review set forth in the FDCA, 21 U.S.C. § 355(c) also constitutes final agency action reviewable under the APA as agency action unlawfully withheld. *See* 5 U.S.C. §§ 551, 704, 706; *Sandoz, Inc. v. Leavitt*, 427 F. Supp. 2d 29, 34 (D.D.C. 2006).

40. There is no statutorily mandated requirement that Avadel seek relief from the Agency before bringing suit in this Court. Thus, administrative exhaustion is not a prerequisite to suit.

41. In any event, immediate judicial review is warranted for the very reason that Avadel has already made exhaustive efforts to obtain relief from FDA to no avail.

42. Specifically, Avadel has repeatedly requested FDA take action on the LUMRYZ NDA consistent with governing law and has addressed all issues that FDA has raised regarding LUMRYZ's approvability. Despite these communications, FDA issued its Patent Decision ordering Avadel to submit a certification to the '963 patent and issued a tentative approval, but, to date, has still failed to finally approve or offer a hearing on the approvability of the LUMRYZ NDA. Avadel faces significant and irreparable harm from Defendants' actions, and Avadel has no other adequate remedy.

BACKGROUND

A. Legal Framework for New Drug Applications

43. The FDCA generally prohibits the sale of a "new drug" unless it has been proven safe and effective. 21 U.S.C. § 355(a). 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.*

44. 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 studies or 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.*

45. 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.* But a Section 505(b)(2) applicant must also, under certain circumstances, file a "patent certification" or a "patent statement" regarding certain patents pertaining to the previously approved drug that was subject to the prior investigations. 21 U.S.C. §§ 355(b)(2)(A), (b)(2)(B).

46. 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 so, the applicant must make 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).

47. The statute also provides an alternative pathway for Section 505(b)(2) applicants to identify patents that do not fall within certification categories (i) through (iv), *i.e.*, a "patent statement."

48. Specifically, if a 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).

49. 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 Caraco Pharm. Laby's, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405–06 (2012).

50. 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).

51. 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 to determine whether they accurately reflect the patented drugs and uses. *See Caraco*, 566 U.S. at 405; *Purepac Pharm. Co.*, 238 F. Supp. 2d at 196. Instead, FDA has assumed a "purely

ministerial" role, and "simply lists the patent information that it receives from brand manufacturers . . . ." *Purepac*, 238 F. Supp. 2d at 196.

52. 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 197. 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 to render that information accurate. *Id.* (quoting 21 C.F.R. § 314.53(f)).

53. A certification may affect the date that FDA's approval of a new drug takes effect. For example, if a "paragraph IV" certification is filed claiming that "such patent is invalid or will not be infringed" by the new drug, approval will not be made effective for a "thirty-month period" 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).

54. Absent another limitation on approval (such as the stay referenced above), FDA has a mandatory statutory duty to approve an NDA 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." *Id.* § 355(c)(1)(A), (d).

55. 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

56. 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.

57. 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.*

58. FDA has discretion to determine whether a REMS is necessary "to ensure that the benefits of the drug outweigh the risks of the drug." 21 U.S.C. § 355-1(a)(1). In making that determination, FDA considers multiple factors, including the benefits of the drug to patients, and the "seriousness of any known or potential adverse events that may be related to the drug." *Id.*

59. 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"). *See In re Xyrem (Sodium Oxybate) Antitrust Litig.*, 555 F. Supp. 3d 829, 841 (N.D. Cal. 2021).

60. Notably, Jazz has, for many years, used its REMS and REMS-related patents to maintain its monopoly over oxybate products. *See In re Xyrem*, 555 F. Supp. 3d at 840–44. 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).

61. 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-related patents. *See generally* Compl., *Jazz Pharm., Inc. v. Roxane Laby's, Inc.*, C.A. No. 10-6108 (D.N.J. 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 oxybate drugs.

62. In 2017, FDA criticized the "inconsistent position[s]" Jazz has taken with respect to multiple aspects of its REMS over the years, which have "suggest[ed] Jazz's knowledge" that its REMS "could have the effect of preventing [ ] competition" for sodium oxybate products." *In re Xyrem (Sodium Oxybate) Antitrust Litig.*, No. 20-MD-02966-LHK, 2021 WL 3612497, at *6 (N.D. Cal. Aug. 13, 2021 (quoting Mem. from Trueman Sharp, Deputy Director for the Office of Generic Drugs, FDA, to ANDAs for sodium oxybate oral solution products, *et seq.* (Jan. 17, 2017)).

63. 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 In re Xyrem*, 555 F. Supp. 3d at 841 ("According to Plaintiffs, Jazz's alleged abuse of the REMS process spanned nearly seven years beginning in late August 2008."); 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. FDA's Initial Review of the LUMRYZ NDA

64. On December 15, 2020, Avadel submitted an NDA for LUMRYZ under Section 505(b)(2) of the FDCA.

65. As part of that application, Avadel submitted a proposed REMS, in compliance with 21 U.S.C. § 355-1. Avadel 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. Avadel further submitted patent *statements* pursuant to 21 U.S.C. § 355(b)(2)(B) for five Jazz patents, averring that those patents do not claim a method of using sodium oxybate for which Avadel is seeking approval. Those certifications and statements are not at issue here.

66. Avadel also submitted a patent statement regarding the '963 patent, stating that this patent does not cover a method of using sodium oxybate for which Avadel is seeking approval of LUMRYZ. For the '963 patent, Jazz has submitted a use code, U-1110, for inclusion in the Orange Book, which covers a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution."

67. In its patent statement, Avadel explained that U-1110 does not cover any drug substance, drug product, or method of use such that any patent certification would be required, because the '963 patent's claims, according to U-1110, are directed to the use of a computer database in a computer system, not a drug, and Avadel's proposed labeling for LUMRYZ describes no such requirement. Moreover, the statement explained, the proposed LUMRYZ REMS was "materially different" from the Xyrem REMS described in U-1110, because the LUMRYZ REMS

"utilizes multiple secure, validated, separate, and distinct databases (as opposed to 'a computer database')," *i.e.*, the single, centralized database covered by U-1110 and the '963 patent.[1]

68. 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." The NDA was therefore deemed filed as of February 13, 2021 "in accordance with 21 CFR 314.101(a)," meaning that FDA's review was required to be complete by August 12, 2021. 21 U.S.C. § 355(c); 21 C.F.R. § 314.101(a)(2).

69. 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."

70. Avadel assented to that extension of FDA's time for review to October 15, 2021. 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]

72. [redacted]

[1] On March 25, 2022, Avadel sent FDA an updated patent statement, with materially identical content as the original statement regarding the '963 patent.

[redacted]

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

73. [redacted]

74. Since the October 15, 2021, PDUFA date, Avadel has 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.

75. 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. They certainly provide no explanation for FDA's many months of delay.

76. What followed were months of delay in which Avadel repeatedly sought clarity on when FDA's final decision would issue, but FDA declined to provide a revised deadline for its review.

[redacted]

[redacted]

80. [redacted]

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

81. On May 24, 2022, 221 days after its statutory deadline to render a final decision on the LUMRYZ NDA as a whole, 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 final decision on one aspect of the NDA in FDA's Patent Decision.

82. The Patent Decision 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."

83. FDA ordered Avadel to "provide an appropriate patent certification under 21 CFR 314.50(i)(1)(i) to address the '963 patent." FDA explained that its Patent Decision "constitutes a final decision" from FDA requiring Avadel to submit a patent certification.

84. In its Patent Decision, FDA evaluated whether the LUMRYZ NDA seeks "approval for the protected use described in the U-1110 use code." To determine this "use" in the LUMRYZ NDA, FDA looked not only at the LUMRYZ prescribing information but also at a "LUMRYZ REMS document," because the former purportedly "did not provide the complete description of all the LUMRYZ REMS program requirements."

85. 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.'"

86. FDA compared this "Lumryz REMS documents" to the "face" of the U-1110 code, which describes the use of "*a* computer database." (emphasis added).

87. Without reference to any authority, and refusing the apply the ordinary English language, FDA "interpret[ed] 'a' computer database to refer to any—one or more—computer databases."

88. Based on this capacious reading of U-1110, the Patent Decision 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.

89. Accordingly, the Patent Decision 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.

90. FDA explained that its Patent Decision "constitutes a final decision" requiring Avadel to submit a patent certification to the '963 patent.

91. On June 6, 2022, Avadel filed a paragraph IV patent certification to the '963 patent, as FDA had ordered it to do, but did so under protest, emphasizing that Avadel maintained that its initial Section 355(b)(2)(B) patent statement regarding Jazz's REMS patent was proper, and that Avadel believed FDA's determination that it could not approve LUMRYZ without a certification

to that patent was erroneous. Avadel explained that it would withdraw its patent certification to the '963 patent should the Patent Decision be set aside.

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

92. Six weeks later, on July 18, 2022, FDA issued its 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."

93. 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. 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. *See* 21 C.F.R. § 314.105(a).

94. 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."

95. 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." *See also* 21 U.S.C. § 355(c)(3)(C). 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 . . . ." *See also* 21 U.S.C. § 355(c)(3)(C).

96. However, 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.

97. Due to FDA's Patent Decision and the resultant certification to the '963 patent under protest, this lawsuit triggered the stay identified by FDA. 21 U.S.C. § 355(c)(3)(C). That stay now precludes the immediate approval of the LUMRYZ NDA, as would have otherwise been possible in July 2022, 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).

98. By contrast, were FDA's Patent Decision to be vacated, there would be no remaining obstacle to final approval of the LUMRYZ NDA, as FDA itself identified in its Tentative Approval.

99. On July 21, 2022, Avadel filed this Complaint to remedy FDA's violation of the FDCA through its Patent Decision.

G. Harm Caused By FDA's Unlawful Failure To Approve LUMRYZ

100. As a direct and proximate result of FDA's Patent Decision, Avadel will face substantial and irreparable harm.

[redacted]

104. [redacted]

[redacted]

106. LUMRYZ is Avadel's sole product candidate. Avadel has no other prospective revenue streams. Avadel has spent almost a decade, [redacted], and virtually all of its resources on the development of LUMRYZ.

[redacted]

[redacted]

CLAIMS FOR RELIEF

CLAIM I: VIOLATION OF THE ADMINISTRATIVE PROCEDURE ACT AGENCY ACTION THAT IS ARBITRARY, CAPRICIOUS, AN ABUSE OF DISCRETION, NOT IN ACCORDANCE WITH LAW, IN VIOLATION OF STATUTORY RIGHT, IN EXCESS OF STATUTORY AUTHORITY
Violation of 5 U.S.C. § 706; 21 U.S.C. § 355(b)(2); 21 C.F.R. § 314.50

119. The foregoing paragraphs are incorporated by reference as if set forth in full herein.

120. The Administrative Procedure Act prohibits Defendants from acting in any way that is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with the law, or that is in excess of statutory jurisdiction or authority or short of statutory right. 5 U.S.C. § 706(2)(A), (C).

121. By statute, the decision whether to file a patent certification under § 355(b)(2)(A) or a patent statement under § 355(b)(2)(B) rests solely in the "opinion" of the new drug "applicant," here Avadel.

122. Avadel chose to submit a patent statement regarding Jazz's '963 patent described in the U-1110 use code, certifying that Jazz's '963 patent as described in U-1110 does not "claim[ ] a use for such drug for which the applicant is seeking approval."

123. Defendants lack any statutory authority to second-guess Avadel's decision to file a patent statement, rather than a patent certification, under 21 U.S.C. § 355(b)(2)(B).

124. FDA's Patent Decision compelling Avadel to submit a patent certification instead of a patent statement otherwise lacks any sound legal basis.

125. First, the use code U-1110 does not describe the use of any drug, much less sodium oxybate, as required by Section 355(b) to trigger a patent certification.

126. Second, to determine the scope of an NDA's proposed use for a drug, Defendants are confined by regulation to examining the "labeling" of the drug. 21 C.F.R. § 314.50(i)(1)(iii)(B). Defendants unlawfully violated their own regulations in the Patent Decision by looking beyond LUMRYZ's labeling to an extrinsic "LUMRYZ REMS document," to find that Avadel was seeking approval for a "use" that overlapped with U-1110 and therefore that Avadel was required to submit a patent certification with respect to the '963 patent.

127. Third, Jazz's use code, U-1110, purports to cover only a "method of treating a patient with a prescription drug using a computer database in a computer system for distribution." But Avadel, through the LUMRYZ NDA, does not seek a "method of treating a patient with a prescription drug using *a computer database in a computer system* for distribution," as provided for in U-1110; Avadel's proposed LUMRYZ REMS will utilize multiple computer databases to implement the LUMRYZ REMS.

128. For the foregoing reasons, Defendants' Patent Decision, ordering Avadel to submit a patent certification with respect to the '963 patent, is arbitrary, capricious, an abuse of discretion, not in accordance with law, in excess of statutory jurisdiction and authority, and short of statutory right.

CLAIM II: VIOLATION OF THE ADMINISTRATIVE PROCEDURE ACT AGENCY ACTION UNLAWFULLY WITHHELD Violation of 5 U.S.C. § 706; 21 U.S.C. § 355(b)(2)

129. The foregoing paragraphs are incorporated by reference as if set forth in full herein.

130. The Administrative Procedure Act prohibits Defendants from unlawfully withholding agency action. 5 U.S.C. § 706(1).

131. Defendants had a nondiscretionary legal duty, within 180 days after the filing of the LUMRYZ NDA or within such additional time agreed upon between FDA and Avadel (*i.e.*, October 15, 2021), to either approve the LUMRYZ NDA or give Avadel notice of an opportunity

for a hearing before the HHS Secretary regarding whether the LUMRYZ NDA is approvable. 21 U.S.C. § 355(c).

132. Defendants have no discretion to refuse to act on the LUMRYZ NDA, nor do Defendants have discretion to indefinitely retain the LUMRYZ NDA without issuing a final decision granting final approval or offering a hearing. *See id.*; *Sandoz*, 427 F. Supp. 2d at 36–37.

133. Defendants' failure to act on the LUMRYZ NDA by granting final approval of the LUMRYZ NDA or offering a hearing on the final approvability of LUMRYZ is thus contrary to law and constitutes "agency action unlawfully withheld." 5 U.S.C. § 706(1).

134. Neither the issuance of the Patent Decision nor the Tentative Approval, neither of which granted final approval to the LUMRYZ NDA or authorized Avadel to bring LUMRYZ to market, relieves Defendants of their independent and mandatory statutory obligation to timely grant final approval of the LUMRYZ NDA or provide a hearing on the approvability of the LUMRYZ NDA. *See* 21 U.S.C. § 355(c).

135. For the foregoing reasons, FDA should be directed to take final action on the LUMRYZ NDA within 14 days of the Court's order.

REQUEST FOR RELIEF

Avadel respectfully requests that the Court enter judgment in its favor and grant the following relief:

1. A declaration pursuant to 28 U.S.C. § 2201 that:

   a. Defendants' Patent Decision ordering Avadel to submit a certification to the '963 patent violates 21 U.S.C. § 355 and 21 C.F.R. § 314.50;

   b. Defendants' Patent Decision ordering Avadel to submit a certification to the '963 patent is arbitrary, capricious, an abuse of discretion, not in accordance

with law, in excess of statutory jurisdiction and authority, and short of statutory right, *see* 5 U.S.C. § 706(2);

c. Defendants violated the mandatory statutory deadline in 21 U.S.C. § 355 by failing to finally approve or offer a hearing on the approvability of the LUMRYZ NDA by October 15, 2021, and accordingly agency action has been and continues to be unlawfully withheld, *see* 5 U.S.C. § 706(1);

2. An order setting aside and vacating FDA's May 24, 2022 Patent Decision;

3. Injunctive relief enjoining Defendants from requiring Avadel to submit a patent certification to the '963 patent, including as a precondition to NDA approval;

4. An order directing FDA to take final action on the LUMRYZ NDA within 14 days of the Court's order, *see* 5 U.S.C. § 706(1); and

5. Such other and further relief as the Court deems just and proper.

Respectfully submitted,

Dated: July 21, 2022

/s Philip J. Perry

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