No. 2023-1186

In the

United States Court of Appeals for the Federal Circuit

JAZZ PHARMACEUTICALS, INC.,

Plaintiff-Appellant,

v.

AVADEL CNS PHARMACEUTICALS LLC,

Defendant-Appellee.

Appeal from the United States District Court
for the District of Delaware, Gregory B. Williams, J.

BRIEF OF THE PUBLIC INTEREST PATENT LAW INSTITUTE, PROFESSOR ROBIN FELDMAN, NARCOLEPSY PATIENTS, AND THE NISKANEN CENTER AS *AMICI CURIAE* IN SUPPORT OF DEFENDANT-APPELLEE

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CERTIFICATE OF INTEREST

Pursuant to Rules 29(a) and 47.4 of the Federal Circuit Rules of Practice, counsel certifies as follows:

(1) The full name of every party or amicus represented by me is **the Public Interest Patent Law Institute, Professor Robin Feldman, Eliana Bookbinder, Brian Mahn, and the Niskanen Center**.

(2) The above-identified parties are the real parties in interest.

(3) The corporate disclosure statement of Rule 26.1 of the Federal Rules of Appellate Procedure is as follows: There is no parent corporation to or any corporation that owns 10% or more of stock in the above-identified parties.

(4) The names of all law firms and the partners and associates that have appeared for the party in the lower tribunal or are expected to appear for the party in this court, not including those who have entered or are expected to enter an appearance before this court, are: **None**.

(5) The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal are: **None other than that identified in Appellee's brief**.

(6) All information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees): **None**.

Dated: January 18, 2023

/s/ David Bookbinder
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Cases

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Other Sources

Abbreviated New Drug Application Regulations, 59 Fed. Reg. 50338 (Food & Drug Admin. Oct. 3, 1994) 16

Answer to Complaint for Patent Infringement, Defenses and Counterclaims, *Jazz Pharm., Inc. v. Avadel CNS Pharm., LLC*, No. 1:21-cv-691 (D. Del. Nov. 18, June 3, 2021) (Doc. No. 11) 11

Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36675 (Food & Drug Admin. June 18, 2003) 15

Robert H. Bork, *The Antitrust Paradox* (1978) 18

Susan A. Creighton et al., *Cheap Exclusion*, 72 Antitrust L.J. 975 (2005) . . . 18

Agata Dabrowska, Cong. Research Serv., *Report No. R44810*, *FDA Risk Evaluation and Mitigation Strategies (REMS): Description and Effect on Generic Drug Development* (Mar. 16, 2018) 22

Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 Tex. L. Rev. 685 (2008–2009) 17–18

Drug Enf't Admin., U.S. Dep't of Justice, *Drug Fact Sheet* (Apr. 2020), https://www.dea.gov/sites/default/files/2020-06/GHB-2020_0.pdf 4

Charles Duan, *Mandatory Infringement*, 75 Fla. L. Rev. (forthcoming 2023), https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4193947 . . . . 17, 19

Federal Trade Commission's Brief as *Amicus Curiae*, *Jazz Pharm., Inc. v. Avadel CNS Pharm., LLC*, No. 1:21-cv-691 (D. Del. Nov. 18, Nov. 15, 2022) (Doc. No. 227) 21

Food & Drug Admin., *Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book)* (42d ed. 2022), https://www.fda.gov/media/71474/download 14

Michael A. Gollin, *Using Intellectual Property to Improve Environmental Protection*, 4 Harv. J.L. & Tech. 193 (1991) 18

Thomas J. Holmes et al., *Monopoly and the Incentive to Innovate When Adoption Involves Switchover Disruptions*, 4 Am. Econ. J.: Microeconomics 1 (2012) 19

Office of Commc'ns & Pub. Liaison, Nat'l Insts. of Health, *Narcolepsy Fact Sheet* (last reviewed Sept. 27, 2022), https://www.ninds.nih.gov/narcolepsy-fact-sheet 5–6

Overdose? Profuse Sweating on Xyrem, Reddit r/Narcolepsy (July 25, 2021), https://www.reddit.com/r/Narcolepsy/comments/or73pp/overdose_profuse_sweating_on_xyrem/ 7

Risk Evaluation and Mitigation Strategies (REMS), U.S. Food & Drug Admin. (last updated Dec. 17, 2021), https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems . . 3

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Wendy H. Schacht & John R. Thomas, *The Hatch-Waxman Act: A Quarter Century Later* (Cong. Research Serv., Report No. R41114, Mar. 13, 2012), https://www.everycrsreport.com/reports/R41114.html 14

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INTEREST OF *AMICI CURIAE*[1]

The Public Interest Patent Law Institute ("PIPLI") is a nonprofit organization dedicated to ensuring the patent system promotes innovation and access for the public's benefit. PIPLI conducts research on patent policy issues, represents the public's interest in courts and agencies deciding issues of patent law, and advocates for transparency, integrity, and accountability throughout the patent system.

Professor Robin Feldman is the Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson '54 Distinguished Professor of Law Chair, and Director of the Center for Innovation at UC College of the Law, San Francisco.[2]

Eliana Bookbinder and Brian Mahn are patients with narcolepsy who take Xyrem or Xywav.[3] They have benefited from the existence of these drugs and are happy that a treatment for their condition is available. However, they are personally familiar with the logistical difficulties associated with taking Xyrem and Xywav and support the entry of new products.

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[1]Pursuant to Federal Rule of Appellate Procedure 29(a), all parties received appropriate notice of and consented to the filing of this brief. Pursuant to Rule 29(c)(5), no counsel for a party authored this brief in whole or in part, and no counsel or party made a monetary contribution intended to fund the preparation or submission of the brief. No person or entity, other than *amici*, their members, or their counsel, made a monetary contribution to the preparation or submission of this brief.

[2]Affiliations are included for identification purposes only.

[3]Jazz recently introduced Xywav, a low-sodium formulation of Xyrem; this brief refers to them collectively as Xyrem.

The Niskanen Center is a nonprofit, nonpartisan 501(c)(3) public policy think tank and advocacy organization working to protect private property rights, economic liberty, well-functioning markets, and to roll back regressive regulations which restrict freedom of exchange and increase inequality. The Niskanen Center believes that the patent system should be a force for progress and should not be used in a manner that prevents free entry and innovation and that U.S. food and drug regulations are not used as a tool to block competition, innovation, patient choice, and better health outcomes for those dealing with narcolepsy.

SUMMARY OF ARGUMENT

Delisting of U.S. Patent No. 8,731,963 ("the '963 patent") from the Orange Book, as the district court ordered, is in the interest of the balance built into the patent system, the intent of the Hatch–Waxman Act, and patients who suffer from narcolepsy. Appellant Jazz Pharmaceuticals makes a useful product, Xyrem, that helps people with narcolepsy and other serious sleep disorders. Appellee Avadel Pharmaceuticals developed a different drug, Lumryz, that improves on Xyrem by addressing some of the drawbacks associated with taking Xyrem.

Xyrem must be taken twice a night: an initial dose at bedtime, and then a second two to four hours later. Ironically, Xyrem requires patients with sleep disorders to wake in the middle of the night, while still under the influence of the first dose. Once-nightly Lumryz eliminates patients' need to rouse themselves from a drug-induced sleep in order to take a second dose. This brief includes the first-hand experiences of Xyrem patients, showing the pressing and immediate need for this improved treatment to be available on the market.

The '963 patent that Jazz asserts to block introduction of Lumryz is directed not to the drug itself, but to a computer system for safe dispensation of a drug.[4] The Food and Drug Administration ("FDA") mandated use of such a safe dispensation

[4] *See generally Risk Evaluation and Mitigation Strategies (REMS)*, U.S. Food & Drug Admin. (last updated Dec. 17, 2021), *available online*. Locations of authorities available online are shown in the Table of Authorities.

system under its Risk Evaluation and Mitigation Strategies ("REMS") authority, because the active ingredient in both Xyrem and Lumryz is sodium oxybate, a controlled substance.[5] Such patent assertions exploiting the regulatory system are uniquely problematic, as they upend traditional expectations of how patents work, give rise to strong market power, and undermine the very innovation incentives that patents are supposed to create.

Jazz maintains that the '963 patent entitles the company to a stay on the approval of Lumryz under the Drug Price Competition and Patent Term Restoration Act ("Hatch–Waxman") as amended. And yet that statute, primarily designed to facilitate the marketing of generic pharmaceuticals rather than to impede novel and improved products, is improperly used here. To achieve the twin goals of patent protection and competition, the statute provides what is effectively a 30-month preliminary injunction for a limited class of patents on active ingredients, drug formulations, and methods of use—none of which characterizes the '963 patent. Allowing patent holders like Jazz—who have not created the kinds of inventions Hatch–Waxman was designed to encourage—to use this remedy undermines the purposes of both Hatch–Waxman and the patent system overall.

[5]The Drug Enforcement Administration lists sodium oxybate as a Schedule I controlled substance, and Xyrem as a Schedule III substance. Drug Enf't Admin., U.S. Dep't of Justice, *Drug Fact Sheet* (Apr. 2020), *available online*.

ARGUMENT

I. Jazz Harms Patients by Blocking a Useful Improvement to Their Treatment

By using the '963 patent to prevent Lumryz's introduction, Jazz harms those it has in the past helped: the 135,000 to 200,000 Americans suffering from narcolepsy and other serious sleep disorders.[6] Xyrem's twice-nightly regimen means users take a sleep-inducing drug that requires them to wake up in the middle of the night in order to take a second dose designed to give them a full night's sleep. Xyrem users are grateful for an often effective narcolepsy treatment, but Xyrem's 2-dose regimen causes serious disruptions in their lives that Lumryz will hopefully eliminate.

To assess the real-world effects for patients, *amici* spoke with several of them about their experiences with Xyrem, and also researched existing online commentary by narcolepsy patients.[7]

A. Xyrem's Double-Dose Schedule Creates Significant Problems for Patients

Taking Xyrem's second dose around four hours after taking the first one means having to wake up while still under the influence of the first dose. The most obvious

[6]Office of Commc'ns & Pub. Liaison, Nat'l Insts. of Health, *Narcolepsy Fact Sheet* (last reviewed Sept. 27, 2022) [hereinafter Narcolepsy Fact Sheet], *available online*.

[7]To maintain the privacy of their specific medical conditions, patients are discussed only anonymously or in the aggregate below.

problem is that having been knocked out by the first dose, patients are often unable to wake for their alarms; patients reported setting multiple blaring alarms, often unsuccessfully, and relying on spouses and family members to wake them up. One patient reported that even after two years of using Xyrem, they miss their second dose about once a week.

If a patient does not wake up for the second dose, they may then wake up after about five or six hours of sleep. This creates a dilemma for patients. The patient can skip their second dose and suffer the symptoms of narcolepsy resulting from lack of sleep. Missing the second dose means, in the words of one patient "wak[ing] up tired, achey, [and in a] bad mood." Missing the second dose can also lead to rapid-onset drowsiness and cataplexy attacks—the sudden onset of "weakness and a loss of voluntary muscle control".[8]

Alternatively, patients who have not woken up on schedule can take their second dose late, forcing them to oversleep. Whether or not the patient successfully wakes up and times their dosage correctly, a second problem emerges: patients are often groggy and disoriented—in no condition to measure out a precise volume of the liquid Xyrem formulation—meaning that the second-dose routine must be carefully orchestrated in advance. One patient measured out the second dose before bed but feared that the family pets might knock over the container; another

[8]Narcolepsy Fact Sheet, *supra* note 6.

reported receiving a concussion from falling over in the process of taking the second dose. Another patient reported falling asleep in the bathroom when going to take the second dose.

Even worse is when a patient wakes up early, as can happen when the first dose is not titrated precisely or the patient's daytime activities cause a change in sleep patterns. Ideally, the patient realizes the error and is subjected to staying awake for hours until it is the right time to take the second dose. But being half-asleep in the middle of the night, some patients reported not realizing what time it was and taking the second dose early, effectively overdosing on Xyrem. One patient recalled realizing they had taken the second dose early, and panickedly tried to monitor for overdose symptoms by staying awake while on the double-dose of sleep medication. Adding to the complexity of mistiming the second administration of Xyrem is the fact that these decisions are made under the influence of the first dose of Xyrem in the wee hours of the morning.[9]

B. The Drug's Complexity Has Caused Personal and Professional Losses

Structuring one's life around a twice-nightly drug and fearing dosage errors, unsurprisingly, exacts a toll. One patient compared the lifestyle changes required to take Xyrem to those associated with being diabetic. The patients *amici* spoke

[9] *See also Overdose? Profuse Sweating on Xyrem*, Reddit r/Narcolepsy (July 25, 2021), *available online*.

to discussed how Xyrem's complicated dosing regimen had cost them personally and professionally.

Families of patients bear an immense burden. One patient relied on their parents to wake them up for their second dose (alarms did not work for them); the patient said they were immensely thankful to have family around to help but felt bad for making them wake up every night. Marriages have ended in divorce and students could not find roommates, we were told, because of the disruptive nightly second-dose routine. One patient wondered how a Xyrem patient could ever have children, as the drug's strict schedule regimen would seem incompatible with the unpredictable midnight needs of infants and toddlers.

Patients' careers and education also often suffered. Xyrem patients face more than the general inconveniences associated with oversleeping: if they are still experiencing the effects of Xyrem when they wake up it is unsafe to drive a car to get to work or school. Delayed second doses made patients late for school or work. One patient we talked to was a college student at the time they started taking Xyrem and reported not being able to enroll in morning courses because they might miss class due to a delayed second dose. One patient lost their job, another contemplated dropping out of school, and third could barely find time to do homework.

C. Patients Often Feel Unheard

The opportunity to take a once-nightly formulation excited the patients *amici* spoke to, given their longstanding difficulties with the twice-nightly Xyrem formulation. These patients anticipated that Avadel's once-nightly formulation would tremendously improve their quality of life beyond the benefits they already receive from having a drug, Xyrem, to treat their narcolepsy. One patient mentioned the simple joy of having mornings where they can have breakfast after a predictable night of sleep. Others anticipated relieving burdens on their families, being able to work, traveling freely, and thinking of children and pets as companions rather than as risks to the medication regimen.

Given these tremendous benefits for patients, one would think that Jazz would have had strong incentives to develop its products to satisfy demand. And yet many of the patients intimated (or said outright) that Jazz insufficiently prioritized patient welfare. One complained that Jazz's distribution restrictions had become more burdensome over time, making it increasingly difficult for them to receive treatment. Surprisingly, one patient, attending a national narcolepsy conference, found no Jazz representatives delegated to meet with patients there.

Patients also reported difficulties with another aspect of Xyrem: the complex delivery and distribution process required under the REMS program. Patients had to stay home from work to sign for shipments of their medications, and had

difficulty finding providers and pharmacies authorized to prescribe and dispense Xyrem. Jazz distributes Xyrem using FedEx, and requires receipt by someone over the age of 21. This is inconvenient for those who either live alone, with someone who is out during the day, or who have trouble receiving such sensitive packages via their apartment, workplace, or dormitory mail room. One of the patients found a workaround to this system by asking FedEx to hold the package at their facility. This way, they could pick up Xyrem in the same way they would go to a pharmacy to pick up a drug. But Jazz does not offer that option to patients: instead, they must use FedEx's system to ask for the package to be held.

The patients we talked to were clear that they did not think Xyrem was a bad product: many of them used it successfully or knew of others who did so. One gave it a ringing endorsement when they described it as "amazingly effective" in the treatment of narcolepsy. What was ultimately of concern to them was patient choice. Narcolepsy affected each of them differently, and the lifestyle choices imposed by Xyrem worked for some patients and not others, we were told. Having new and different sodium oxybate products on the market, especially ones that addressed patient difficulties such as twice-nightly dosing, was the ultimate outcome that patients hoped would be achieved.

Patients desire an alternative to Xyrem that can also treat their narcolepsy without the side effects of their current medication. The practical benefits of improved

choice in and access to medication should inform this Court's decision to affirm the district court's order.

II. A Healthy Drug Patent System Relies on Judicial Oversight of Orange Book Listings

A. An Improperly Listed Orange Book Patent Interferes with the Development and Utilization of Medicines

Bringing a new drug to market is no mean feat, especially if that drug can be abused and requires the FDA to approve a REMS for it. Avadel sought FDA's approval for Lumryz, including the development of a REMS. Avadel worked with the FDA to develop a REMS modeled after one previously approved for Jazz, and Lumryz was tentatively approved pending certification that Lumryz did not infringe on any patents in the Orange Book.

After receiving a complaint for infringement of the '963 patent (and four others), Avadel filed a counterclaim seeking, among other forms of relief, a requirement by the district court for Jazz to delist the '963 patent from the Orange Book as the '963 patent "only includes claims to a 'computer-implemented system for treatment of a narcoleptic patient with a prescription drug,' which are neither method claims nor claims to a drug product or drug substance." Answer to Complaint for Patent Infringement, Defenses and Counterclaims at 41, *Jazz Pharm., Inc. v. Avadel CNS Pharm., LLC*, No. 1:21-cv-691 (D. Del. Nov. 18, June 3, 2021) (Doc. No. 11).

The question presented to the Court is whether or not to uphold the Delaware District Court's order for Jazz Pharmaceuticals to delist its patent covering a required REMS because the patent covers neither a "drug substance (active ingredient) . . . a drug product (formulation composition) [or a] method of using such drug." Federal Food, Drug, and Cosmetic Act (FFDCA) § 505(b)(1)(A)(viii), 21 U.S.C. § 355. The district court found that the '963 patent "does not belong in the Orange Book." Given the unambiguous finding by the district court and the harm of granting Jazz what is effectively a 30-month preliminary injunction, this Court should affirm the district court's order.

Instead of covering an invention that can be statutorily submitted to the Orange Book, the '963 patent covers the use of a REMS. Because Avadel's product at issue here uses the same active ingredient as Jazz's product, sodium oxybate, the FDA requires a REMS for the drug. The '963 patent is described as a "sensitive drug distribution system and method" claiming, "A *computer-implemented* system for treatment of a narcoleptic patient with a prescription drug that has a potential for misuse, abuse or diversion, comprising prescriptions for a sensitive drug." A drug, active ingredient, formulation, composition, or method of using the drug are not mentioned. *See id.*

The erroneous listing of the '963 patent in the Orange Book creates a unique problem for those like Avadel that want to develop novel therapies that compete

with Xyrem by offering a product, Lumryz, that is an improvement over Jazz's. Lumryz represents a significant step forward in treating narcolepsy and the innovation offers greater choice to patients who suffer from it.

An automatic 30-month delay goes well beyond the normal injunctive relief available to those claiming patent infringement. Avadel developed a new product to address a real need by patients and took all the necessary steps to ensure the product is available safely. This is what a well-functioning pharmaceutical industry looks like. The Court should not allow Jazz to interrupt this process by using the special rights granted to it by a patent that is incorrectly placed in the Orange Book.

B. Keeping the '963 Patent in the Orange Book Undermines the Balance Created in the Hatch-Waxman Act

The patent system exists to "promote the Progress of . . . useful Arts," by authorizing the grant of exclusive rights over new inventions. U.S. Const. art. I, § 8, cl. 8. These inventions include pharmaceutical products, an industry that relies heavily on the patent system. Pharmaceutical innovations rely on Hatch–Waxman.[10] The law "established several practices intended to facilitate the marketing of generic

[10]Drug Price Competition and Patent Term Restoration Act (Hatch–Waxman), Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at FFDCA § 505). Throughout this brief, "Hatch–Waxman" will refer to the statutory framework as subsequently amended. *See* Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066; Orange Book Transparency Act of 2020, Pub. L. No. 116-290, 134 Stat. 4889.

drugs while permitting brand name companies to recover a portion of their intellectual property rights lost during the pharmaceutical approval process."[11] Among these practices intended to strike a balance between new drug entry and protecting intellectual property rights is a special process for treating patents associated with improved pharmaceuticals, documented in what is commonly called the "Orange Book."[12]

Despite granting a temporary period of exclusivity in exchange for the development and disclosure of an invention, the Patent Act and the larger body of patent law contain provisions to facilitate competition through the provision of injunctive relief not automatically, but "in accordance with the general principles of equity." 35 U.S.C. § 283. Following this requirement of equitable considerations, this Court has repeatedly held that "[a] plaintiff seeking a preliminary injunction must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest." *See Takeda Pharm. USA v. Mylan Pharm. Inc.*, 967 F.3d 1339, 1345 (Fed. Cir. 2020) (citing *Winter v. Nat. Res. Def. Council, Inc.*, 129 S. Ct. 365, 20 (2008)); *Titan Tire*

[11] Wendy H. Schacht & John R. Thomas, *The Hatch-Waxman Act: A Quarter Century Later* 1 (Cong. Research Serv., Report No. R41114, Mar. 13, 2012), *available online*.

[12] *See* Food & Drug Admin., *Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book)* (42d ed. 2022), *available online*.

Corp. v. Case New Holland, Inc., 566 F.3d 1372, 1375–76 (Fed. Cir. 2009); *Apple, Inc. v. Samsung Elecs. Co.*, 678 F.3d 1314 (Fed. Cir. 2012). The Federal Circuit has also acknowledged the importance of deference to district court in determining whether or not to provide injunctive relief. *See Apple*, 678 F.3d at 1323 ("The decision to grant or deny a preliminary injunction lies within the sound discretion of the district court, and we will not reverse its judgment absent an abuse of that discretion.") (citing *Titan Tire*, 566 F.3d at 1375).

The 30-month stay made available under Hatch–Waxman is a departure from this generally equitable approach. The rights afforded to those with a patent in the Orange Book are, by design, a tool to protect the exclusive rights granted to patent holders by allowing them to block entry by would-be competitors beyond those normally available in other cases of alleged infringement. Such rights were conferred as part of a general program designed to speed new drug entry and is part of the tradeoffs built into that system. But as a tradeoff, it was not designed merely as a way to beef up injunctive relief. Hatch–Waxman restricts patents eligible to receive this protection to patents on "a drug substance (active ingredient)[,] a drug product (formulation or composition)[,] or a method of using such a drug." FFDCA § 505(b)(1)(A)(viii).

The FDA's role in the administration of the Orange Book is "ministerial"[13]

[13]Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36675, 36683 (Food & Drug Admin. June 18, 2003).

and "does not have the expertise or the desire to become involved in issues concerning patent law and sufficiency of notice."[14] It is then left to the judiciary to ensure that patents listed in the Orange Book belong there. Hatch–Waxman tolerates this hands-off approach from the FDA by building in a mechanism to resolve improperly listed Orange Book patents. In 2003 Congress passed the Medicare Prescription Drug, Improvement, and Modernization Act of 2003. *See* Pub. L. No. 108-173, 117 Stat. 2066. This updated the Hatch–Waxman framework by creating the opportunity for an applicant to file a counterclaim and receive an order from a district court for the patent holder to "correct or delete the patent information submitted by the holder [if] that patent does not claim either . . . the drug for which the application was approved [or] an approved method of approving the drug." FFDCA § 505(c)(3)(D)(ii)(I).

This balance was carefully crafted to help patients by making it possible for drugs like Lumryz to enter the market. The responsibility to prevent outcomes contrary to the intent of Hatch–Waxman falls to the district court, a responsibility it fulfilled. Reversing the district court's delisting order would undermine the balance built into the framework of Hatch–Waxman.

[14] Abbreviated New Drug Application Regulations, 59 Fed. Reg. 50338, 50350 (Food & Drug Admin. Oct. 3, 1994).

III. Jazz's Unusual Patent Here Undermines Innovation Rather Than Advancing It

The question presented to this Court has significant ramifications for the interaction between the United States' patent and regulatory systems. Jazz's patent exploits the regulatory system in a well-known but distinct manner, giving rise to actual monopoly power and the innovation disincentives that arise therefrom. The district court's finding that the '963 patent does not belong in the Orange Book should be sufficient to uphold the district court's order. Yet this case has broader implications that the Court should take into consideration in its ruling.

A. Jazz's Patent Exploits the Regulatory System, Creating a "Mandatory Infringement" Situation

To understand why the '963 patent is uniquely problematic to innovation, competition, and patients, it is first necessary to observe that it is no ordinary patent. Instead, it is a patent designed to exploit regulatory and public safety systems in a way that, unlike the mine-run of patents, confers extraordinary monopoly power at the expense of public health and welfare.

Scholars have characterized patents that overlap with the regulatory system as "regulatory gaming" or, because competitors must infringe the patent to comply with the regulation, "mandatory infringement." *See* Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 Tex. L. Rev. 685 (2008–2009); Charles Duan, *Mandatory Infringement*, 75 Fla. L. Rev. (forthcoming 2023), *avail-*

able online. Typically, the government mandate has little to do with innovation policy, generally being designed to promote public safety or societal welfare. Mandatory infringement involves the collision of patent policy with other, siloed, governmental policies that each pursue a separate public interest goal. This Court should take into consideration this complicated dynamic and the impossible situation companies like Avadel find themselves in when trying to navigate both the regulatory state and the patent system.

B. Exploiting the Regulatory System Lets Jazz Engage in Anticompetitive Behavior

The mandatory-infringement nature of the '963 patent is critical because it radically alters the usual relationship between patents, competition, and innovation. The basic observation in an extensive literature is that the holder of a patent on a regulatory mandate goes from a mere advantaged competitor in a larger market to a full-blown monopolist. *See, e.g.,* Dogan & Lemley, *supra*, at 687–88; Michael A. Gollin, *Using Intellectual Property to Improve Environmental Protection*, 4 Harv. J.L. & Tech. 193, 219 n.128 (1991) (describing such patents as a "supermonopoly"); *see also* Robert H. Bork, *The Antitrust Paradox* 159 (1978) ("predation by abuse of governmental procedure"); Susan A. Creighton et al., *Cheap Exclusion*, 72 Antitrust L.J. 975, 990–92 (2005). This increase in market power happens because the regulatory mandate constrains the competitive market space

to the scope of the patent, precluding design-around competition and giving the patent holder true market power. *See* Duan, *supra*, at 30–36.[15]

Contrast this with the dynamic that usually exists in markets where innovation—and thus patenting—is extensive. Usually, "[t]he opportunity to charge monopoly prices—at least for a short period—is what attracts 'business acumen' in the first place; it induces risk taking that produces innovation and economic growth." *Verizon Commc'ns Inc. v. Law Offices of Curtis V. Trinko, LLP*, 540 U.S. 398, 407 (2004). But once such a position has been achieved, that incentive no longer exists because those returns can already be counted on, and further investment would not achieve greater returns. *See* Thomas J. Holmes et al., *Monopoly and the Incentive to Innovate When Adoption Involves Switchover Disruptions*, 4 Am. Econ. J.: Microeconomics 1, 3 (2012) ("a firm with a lucrative monopoly may decide not to adopt a technology that, in the short run, disturbs its lucrative position."). The ability to legally block any competition from rivals also enables nonresponsiveness to the needs of consumers.

[15]The overlap with regulation thus distinguishes mandatory-infringement patents from ordinary patents that typically do not confer market power, because ordinarily competitors are not constrained by regulation and so can design around patents to satisfy consumer demand. *See* U.S. Dep't of Justice & Fed. Trade Comm'n, *Antitrust Guidelines for the Licensing of Intellectual Property* 4 (1995), *available online*, *quoted in Ill. Tool Works Inc. v. Indep. Ink, Inc.*, 547 U.S. 28, 45 (2006).

The context of this case provides some evidence to support these observations about competition and market power. In the case of Xyrem, the only substantial innovation since the introduction of the drug came in the form of a low-sodium formulation Xywav—an improvement to be sure, especially for those who have cardiac issues and must watch their sodium intake. But this improvement is one that allowed Jazz to expand on the *extensive* margins and sell to patients who couldn't take something with a high sodium content without addressing the concerns of patients for whom sodium content was not a primary issue.

Patients' comments demonstrate some of the nonresponsiveness to patient needs associated with a firm holding an unchallenged market position. Improvements to the drug itself to change the dosage from twice- to once-nightly were both possible and a clear area for improvement: yet Jazz forwent the opportunity to invest in such improvements. The inconveniences patients face when actually acquiring lawfully prescribed Xyrem and the lack of responsiveness from Jazz to make it easier for patients to obtain their medication is an example of business conduct disinterested in improving customer service. While some of the frustrations expressed by patients in their dealings with Jazz in section I.C of this brief are unavoidable due to the REMS requirement, this does not mean that every feature is essential or Jazz has no opportunities to improve its customer service.

Taken together, this creates a situation where patients must do without improved treatment options for reasons immaterial to the technical or material realities of innovation. It is one entirely created by anticompetitive abuse of the Orange Book system by Jazz. Even a thirty-month stay is a serious hindrance, as the Federal Trade Commission made clear in its *amicus* brief before the district court:

> An improper listing harms competition and consumers: By listing a patent in the Orange Book and then filing an infringement suit, a brand can block competition for up to two-and-a-half years regardless of the scope or validity of the patent and regardless of whether it meets the statutory listing criteria . . . Consumers suffer both because they are forced to continue paying non-competitive prices and because they are deprived of the ability to choose between products . . . [I]f the '963 patent is improperly listed, it appears to be causing significant harm to competition.

Federal Trade Commission's Brief as *Amicus Curiae* at 14–15, *Jazz Pharm.*, No. 1:21-cv-691 (Nov. 15, 2022) (Doc. No. 227).

This case is not the first time that processes related to REMS compliance have been patented and subsequently used to block free entry of competitors. *See* Ameet Sarpatwari et al., *Using a Drug-Safety Tool to Prevent Competition*, 370 New Eng. J. Med. 1476 (2014). This has been identified as a hindrance to generic entry in the context of shared REMS programs and non-Orange Book patents. While initial development of a REMS is not a simple task, it only involves complying with FDA guidelines and regulations. Subsequent entrants who are required to use the same REMS program, by contrast, face "issues such as cost-sharing, confidential-

ity, product liability concerns, antitrust concerns, and access to a license for elements protected by a patent, and generic drug companies have reported difficulty in trying to develop a single, shared system with brand companies."[16]

The stakes here are higher. Rather than delaying generic competition with an existing drug, abuse of REMS via patent law is stopping a new product. And rather than using the ordinary remedies available to the owners of allegedly infringed patents, the remedy is an automatic 30-month stay of approval. A system that allows what is effectively an automatic preliminary injunction to stop new drugs is one that disserves both patients and the progress of medical science.

C. Blocking Patents Discourage Investment in the Development of Related Products

If Jazz only held patents to a "drug substance (active ingredient) . . . , a drug product (formulation composition) [or a] method of using such drug" as required for listing in the Orange Book, then there would still be opportunities for entry and competition by inducing competitors to "invent around" the new patent by inventing, for example, a new and distinct formulation of sodium oxybate. *See* FFDCA § 505(b)(1)(A)(viii).[17] But, as is the case here, if Jazz holds the exclusive

[16] *See* Agata Dabrowska, Cong. Research Serv., *Report No. R44810*, *FDA Risk Evaluation and Mitigation Strategies (REMS): Description and Effect on Generic Drug Development* 11 (Mar. 16, 2018).

[17] The active ingredient has been known since the 1950s and is plainly unpatentable now.

right to the use of a method required for entry *at all* into the market for sodium oxybate formulations, then all entry into the market is prevented.

What would-be competitor would invest resources in the development of a drug that they could not even sell due to a competitor's patent on the only way to comply with regulations necessary for participation in the market? The promise of a slice of the supranormal profits created by a dominant position encourages investment and entry by competitors who offer a product that is either of superior quality to that consumer or at a lower price. If there is no opportunity to access such profits, then there will not be investment in further development. It is unreasonable to expect a non-infringing competitor to incur the "collateral injury the Hatch-Waxman Act's 30-month stay invariably inflicts." *FTC v. AbbVie Inc.*, 976 F.3d 327, 361 (3d Cir. 2020).

* * *

Lumryz is a story of successful pharmaceutical innovation made possible by the rules established under Hatch–Waxman. Avadel identified a market of patients who have had their lives improved by a drug to treat their condition but dealt with negative side effects from their medication. They stepped in and developed a new product to both treat narcolepsy and address the shortcomings of the previous system.

Had the '963 patent not been listed in the Orange Book, then Avadel would be able to obtain approval of its once-nightly product, enabling patients to enjoy its benefits earlier so long as Avadel accepts the risk of retrospective infringement damages. *See* FFDCA § 505(c)(1). Yet by listing it, Jazz has forced Avadel to wait until the completion of litigation for approval, for up to 30 months. *See id.* § 505(c)(3)(C). The improper use of the statutory stay contravenes the principles of balance in patent law and harms narcolepsy patients. The district court's order to delist the patent should be affirmed.

CONCLUSION

For the foregoing reasons, the decision of the district court should be affirmed.

Respectfully submitted,

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