No. 24-5262

IN THE

United States Court of Appeals for the District of Columbia Circuit

JAZZ PHARMACEUTICALS, INC.,

Plaintiff-Appellant,

v.

ROBERT F. KENNEDY, JR., SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; ROBERT MCKINNON CALIFF, M.D., COMMISSIONER OF FOOD AND DRUGS; UNITED STATES FOOD AND DRUG ADMINISTRATION,

Defendants-Appellees,

AVADEL CNS PHARMACEUTICALS, LLC,

Intervenor for Defendant-Appellee.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF COLUMBIA

BRIEF OF 12 NARCOLEPSY PATIENTS, PUBLIC INTEREST ORGANIZATIONS, MEDICAL PROFESSIONALS, AND PROFESSORS OF LAW AND MEDICINE AS *AMICI CURIAE* IN SUPPORT OF DEFENDANTS-APPELLEES (AMENDED TO ADD FURTHER SIGNATORIES)

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ODA	Orphan Drug Act of 1983
FDA	U.S. Food and Drug Administration
LEMS	Lambert-Eaton Myasthenic Syndrome

INTEREST OF *AMICI CURIAE*

Amici curiae are patients, organizations, medical professionals, and scholars who share a common interest in advancing the law toward better patient health and welfare. New, clinically superior drug products for treating rare diseases and conditions tremendously benefit patients and society, because those products offer choice, competition, and improved patient care. In filing this brief, *amici* hope to make this Court aware of the broad real-world implications of this case, both for narcolepsy patients and for the public interest generally.

Generation Patient is a nonprofit organization that represents young adults with chronic and rare conditions across the United States. Created and led entirely by young adult patients, Generation Patient works to increase the health literacy, patient activation, self-management, and advocacy skills of young adult patients.

SUMMARY OF ARGUMENT

Just two words, "same drug," carry the weight of patient welfare, market competition, and innovation policy. The meaning of this phrase will determine whether companies can forcibly exclude better, life-changing treatments out of the hands of thousands of patients. These stakes cannot be ignored. The Orphan Drug Act can and should be interpreted to improve competitive markets and patients' lives, not to cut patients off from major improvements to their care.

I. "Game-changer," "life changing," "truly a new world," "a way better experience," sleep quality that "hasn't happened since childhood"—these words are how narcolepsy patients have reacted to the promise of once-nightly dosing that Avadel's Lumryz product offers. Avadel's product is a form of sodium oxybate, a drug that helps narcolepsy patients sleep through the night. Jazz's incumbent oxybate products, Xyrem and Xywav, are "twice-nightly," as a single dose lasts only around half a night's sleep so a second dose must be taken usually between midnight and 3 AM. But this makes Xyrem and Xywav practically self-contradictory: They are sleep aids, but patients have to wake up mid-sleep to use them. Lumryz, by contrast, is approved for "once-nightly" dosing, so patients need not interrupt their sleep for a second dose.

Once-nightly is a tremendous difference for patients. Waking up while on a sleep medication to take a second dose of a sleep medication is, in a word,

hard. Patients take convoluted measures to wake up for their second dose, sometimes injuring themselves doing so. And the harms of twice-nightly dosing reach beyond patients to parents, children, friends, classmates, and careers. Most importantly, patients want choices. Oxybate products affect patients in different ways: Some like the lower sodium content of Xywav, for example, while others find its side effects intolerable or care more about once-nightly dosing. Diverse patient experiences reflect the importance of competition over multiple products that serve distinct patient needs.

II. These real-world benefits should inform the interpretation of "same drug" under the Orphan Drug Act of 1983 ("ODA"). This phrase provides for the *scope* of orphan drug exclusivity, namely which products the statute excludes from competition. In analogous areas of market-exclusivity law, scope is carefully tailored to balance interests of innovation, competition, and public welfare. In particular, too broad a scope creates an "innovation disincentive"—a monopolist with market power has no more market share to capture, and so has no incentive to invest in advancements.

Orphan drug exclusivity, too, demands balancing of scope. Jazz proposes reading "same drug" broadly to encompass any drug with the same active moiety, giving the company an effective monopoly over all oxybate products including ones perhaps far better than their own. But this leaves the company with little

reason to invest in breakthrough innovations, like once-nightly dosing, that improve patients' lives but do not increase market share. Competitive pressure from superior products keeps the market moving toward more innovative patient options. Congress enacted the ODA to encourage innovation in orphan drugs, so it would be unreasonable to construe the scope of orphan drug exclusivity without considering downstream innovation, competition, and patient welfare interests.

"Same drug" should be interpreted in light of these multifaceted interests and in light of the many patient benefits described above. Particularly in view of the scientific and technical expertise of the U.S. Food and Drug Administration ("FDA") that gave rise to the clinical superiority standard, this Court should read the plain language of the statute logically such that a clinically superior drug is not the "same drug" as an inferior one. Doing so would best implement the policy goals underlying the ODA, and best promise a brighter future to thousands of narcolepsy patients.

ARGUMENT

I. Narcolepsy Patients Enjoy Substantial, Real-World Benefits from a Once-Nightly Sleep Medication

Although the legal theory and record of this case are intricately technical, the case's potential impact is simple and profound, affecting around 142,000 Americans.[1] If Jazz's suit is successful, then these narcolepsy patients cannot use Avadel's once-nightly product Lumryz, leaving Jazz's twice-nightly Xyrem and Xywav products the only ones available.

To assess the effect of this result, *amici*'s counsel researched narcolepsy patient views on oxybate products.[2] This study revealed three general trends dis-

[1] *See* John Acquavella et al., *Prevalence of Narcolepsy and Other Sleep Disorders and Frequency of Diagnostic Tests from 2013–2016 in Insured Patients Actively Seeking Care*, 16 J. Clinical Sleep Med. 1255, 1257 (2020).

[2] As background information, counsel relied in part on conversations with narcolepsy patients discussed in another *amicus curiae* brief filed with the U.S. Court of Appeals for the Federal Circuit. *See* Brief of the Public Interest Patent Law Institute et al. as *Amici Curiae* at 5–11, *Jazz Pharms., Inc. v. Avadel CNS Pharms., LLC*, 60 F.4th 1373 (Fed. Cir. Jan. 18, 2023) (No. 2023-1186). Counsel has also talked to many patients personally. The specific information used in this brief, however, is drawn from public forums and groups of narcolepsy patients. *See r/Narcolepsy*, Reddit (last visited Oct. 23, 2023), *available online* (noting, as of October 2023, that the forum had 26,000 members and was among the top 3% forums by size on the website); *Narcolepsy Network* (last visited Oct. 23, 2023), *available online*. Because the forum comments are publicly viewable, use of them does not constitute human subjects research. Nevertheless, out of respect for the individual patients' privacy and future ability to dissociate themselves from their comments, citations to usernames or specific URLs are not provided in this brief. Quotes are accurate as of September 2023, and should be findable by searching the forums. Locations of authorities available online are shown in the Table of Authorities.

cussed below: Patients face potentially severe harms from the two-dosing regime, those harms extend to patients social and professional circles, and patients seek a competitive market of multiple treatments.

A. Jazz's Twice-Nightly Products, Requiring Patients to Wake While Using a Sleep Medication, Have Caused Difficulties and Even Injuries

Simple logic suggests the fundamental issue with a twice-nightly oxybate product: Patients take it to help them sleep, yet they must wake up in the middle of the night to take it. Waking up mid-sleep for any reason is difficult enough, but doing so while still drowsy from Xyrem or Xywav is especially hard for many patients. Reflecting the views of many, one patient reported sometimes being "in too much of a fog to realize I'm awake to take the second dose."

To wake up for their second dose, Xyrem and Xywav patients often take drastic, convoluted measures. They set up loud alarm systems, hide the medicine and alarms to make them hard to ignore, and set up all manner of devices under their pillows to shake themselves out of bed. One patient, hoping to provide inspiration for fellow forum members, shared an especially complex system involving wireless near-field-communication tags that had to be scanned in order to turn the alarms off, forcing the patient to be sufficiently awake and self-aware to take the second dose.

Even once they succeed in waking themselves mid-sleep, the problems continue. The physical and mental side effects of oxybate drugs apparently have potent effects on some patients when they are not fully awake. Patients have attributed side effects such as incontinence, sleepwalking, and horrifically lucid nightmares to the two-dose regime.[3] Many patients become intensely hungry at second-dose time; combined with lowered inhibitions from both sleepiness and the drug, one patient regularly raided the refrigerator and ate to excess in the middle of the night.

Having to wake up in the middle of every night while cognitively disoriented is also a recipe for injury. *See, e.g.*, M.H. Bonnet, *Cognitive Effects of Sleep and Sleep Fragmentation*, 16 Sleep S65 (1993); David C. Schwebel & Carl M. Brezausek, *Nocturnal Awakenings and Pediatric Injury Risk*, 33 J. Pediatric Psych. 323 (2008). One patient, disoriented upon waking, hit his head severely on the edge of a metal coffee table. Conscious enough to think of those around him, he wrote out a note: "If I die, it's because I fell off the couch and hit my head when I woke up to take my Xyrem."

And then there is the problem of actually taking the second dose while dazed, drowsy, and still dealing with the first dose's lingering influence. Many patients

[3]To be sure, such side effects may be the result of the drug itself and not of the dosing procedure. However, several patients observed a diminishment in these side effects when they switched.

simply don't wake up in time, leaving them "groggy" or in a "brain fog" the next day. Others forget whether they took the second dose, forcing them to figure out (again, while half-asleep) whether to return to bed possibly unmedicated or to consume another measure and possibly overdose. Accidentally taking the second dose early is common and often requires emergency room attention. *See* Geert Mayer et al., *Long-term Compliance, Safety, and Tolerability of Sodium Oxybate Treatment in Patients with Narcolepsy Type 1: A Postauthorization, Noninterventional Surveillance Study* 4, *in* 41 Sleep No. zsy128 (2018), *available online*; Richard K. Bogan et al., *Efficacy and Safety of Calcium, Magnesium, Potassium, and Sodium Oxybates (Lower-Sodium Oxybate [LXB]; JZP-258) in a Placebo-Controlled, Double-Blind, Randomized Withdrawal Study in Adults with Narcolepsy with Cataplexy* 6, *in* 44 Sleep No. zsaa206 (Mar. 12, 2021), *available online*. One patient had an especially difficult situation: The patient often overslept on the first dose, leading to a late second dose, in turn leading the patient to oversleep in the morning and miss the dosing schedule for a different medication. "And it drives[m]e crazy," the patient remarked.

Eliminating the second dose has long been a dream of many patients. Indeed, some reported resigning themselves to using Xyrem or Xywav "once a night because I was UNABLE to wake up for my second dose." *See also* Sameer D. Saini et al., *Effect of Medication Dosing Frequency on Adherence in Chronic Diseases*, 15

Am. J. Managed Care e22, e27 (2009) (reviewing studies finding increased compliance with once-daily dosing versus multiple-daily dosing); Craig I. Coleman et al., *Dosing Frequency and Medication Adherence in Chronic Disease*, J. Managed Care Pharmacy 534–35 (2012), *available online* (similar). For these patients, getting only half a night of sleep was better than the pain of mid-sleep redosing.

The possibility of once-nightly Lumryz being approved thus had patients "excited" and enthusiastic. Patients who shared their experiences moving from Xyrem or Xywav to Lumryz gladly relayed the benefits they felt: sleep quality that "hasn't happened since childhood for me," waking up "mostly refreshed and without brain fog," elimination of bed-wetting and daytime sleepiness, and lack of disorientation. These patients described the switch as "a way better experience" and in "truly a new world for me." Upon reading of these experiences, another patient hoped to make the switch as well, imagining, "Maybe I can finally have a life!"

B. The Complexity of Twice-Nightly Dosing Taxes Patients' Families, Friends, and Jobs

Waking up at night to take a sleep medication also taxes patients' personal and professional relationships. As a result, the circle of people who benefit from a once-nightly product on the market is wider than the patients themselves.

To begin with, if a patient is setting up multiple blaring alarms to wake up in

the middle of the night, what does this do to a partner sleeping in the same bed? In their comments, many patients lamented forcing their loved ones onto their absurd waking schedule. Some slept in separate bedrooms or struggled to wake themselves up without disturbing their partners. And in some cases, patients had such difficulty rousing themselves for the second dose that responsibility fell on their spouses to wake and medicate them. "My biggest issue with Xyrem/Xywav," wrote one patient, "was not waking up for the second dose and not wanting to rely on my wife to wake me up every night."

Other household members, especially small children, were similarly affected. One patient was "struggling" with twice-nightly dosing when a new grandbaby arrived, and another was "torturing myself on the prescribed titration schedule" in order to have some evening time with their spouse after the kids went to bed. When a graduate student recounted difficulties with a significant other after taking the second dose, a forum member responded that it was easier to live alone—an unfortunate outcome during the socially formative early-adult years when narcolepsy often first manifests.

Patients' job market prospects are no less affected. The possibility of missed or late second doses often makes it impossible for patients to commit to a work schedule, or to know that they will be able to drive to work safely. A restaurant line cook regularly juggled shift schedules due to frequently not waking up for a

second dose of Xywav, and was "[w]orking with my d[octo]r on the new Sodium Oxybate E[xtended]R[elease] ordering," presumably referring to Lumryz. And a 29-year-old starting on Xyrem struggled to figure out how to work an 8-to-5 job, given that the potential hazards of driving six hours after the second dose meant that the patient would have to go to bed at 8 PM, leaving only 2 hours of free time a day. "Is this a normal schedule for people on this drug?" the patient asked. "It seems like that is pretty close to just sleeping and working."

And what if the patient is a child, one of the several thousand with pediatric narcolepsy? *See* Anne M. Morse et al., *Prevalence of Diagnosed Pediatric Narcolepsy in the United States*, 42 Sleep A306, A306 (Apr. 13, 2019), *available online*. Their parents face heavy responsibilities to administer the second dose, often sacrificing their own sleep. One mother recounted a horror story in which her narcoleptic daughter woke early and took the second dose herself—"we spent that night watching her breathing and on the phone to the ER room and looking [for] signs of overdosing on xyrem on the internet." Sleepaway camps are at best an ordeal and more often impossible. Certainly parenting a child with a chronic condition is never easy, but the twice-nightly dosing regime exacts a heavy toll both on parents' well-being and on children's development.

Given these experiences, a once-nightly oxybate product potentially aids both narcolepsy patients and their larger social circles. This Court's decision on the

market availability of this product will help or hinder a broad segment of society.

C. Patients React Differently to Narcolepsy Treatments and Need a Wider Range of Choices on the Market

Certainly responses to the range of oxybate products have not been uniform: Some patients have been satisfied with Xyrem or Xywav and have not had difficulties with the second dose. Yet the diversity of responses points to another key observation: Narcolepsy patients are not all the same. Every patient reacts individually to different oxybate products. Because of these individuated outcomes, patients strongly desire a competitive range of products that can serve their particular needs.

Side effects are a key area of patient diversity. For each of Lumryz, Xyrem, and Xywav, some patients reported weight gain while others lost weight. One patient observed nausea on both Lumryz and Xyrem; the patient intended to keep using Lumryz because "it's the best sleep I've ever gotten." There have similarly been discussions of sleepwalking, incontinence, digestive tract issues, and other side effects with regard to each of the three oxybate products. For just about any side effect and any oxybate product, it was not difficult to find some patients having the side effect and other patients not.

Similarly, patients reported a range of outcomes with respect to their sleep duration on each product. As noted above, many people reported getting more

uninterrupted sleep on Lumryz; one person who had tried all three products reported that "Lumryz has been my favorite thus far." But other patients said that they slept no better or even less on Lumryz. The cause of this was unclear, with some community members wondering whether those patients had learned habits of waking for a second dose, such that they would sleep longer on Lumryz after an adjustment period. But a common view was that different people need different amounts of sleep, which could explain the different responses to each product.

Product formulation preferences were another source of patient response diversity. Jazz makes much of its Xywav product's lower sodium content, as if the sodium levels of Lumryz (or Jazz's own, still-marketed Xyrem) were uniformly unsafe for all patients. Yet while some patients did appreciate lower sodium in their medication, many others could have cared less. One viewed the sodium levels as "negligible i[n]m[y]o[pinion] if you had a somewhat active lifestyle." Another found the sodium content manageable with reasonable diet choices. Still another abhorred Xywav's use of the artificial sweetener sucralose, calling to "wage war" on Jazz for doing so. And one patient, planning on switching to Lumryz, said they "will miss [Xywav's] far lower sodium content, but I'm so bad with my second doses it's a small price to pay."

Choice among products matters to patients for further reasons. Due to the

distribution safety protocols the FDA imposes on oxybate products, Xyrem and Xywav are only available from a single mail-order pharmacy. One patient complained about the knowledgeability of the pharmacy staff, and another could not get access due to living on a military base. Having a different manufacturer's product on the market, one available at multiple pharmacies (as Lumryz is), would almost certainly enhance access to critical treatments for this patient community.

And unsurprisingly, many patients were deeply concerned about costs. Numerous posting threads dealt with strategies for dealing with insurance, difficulties with coupon or rebate programs, and general dissatisfaction with high prices. Many patients hoped that the introduction of Lumryz would improve competitive conditions to the benefit of patients. And a number of patients criticized Jazz's deal with generic oxybate manufacturer Hikma Pharmaceuticals that has kept the generic's prices high, with one commenter feeling that the companies were "using us (Narcolepsy Patients) as leverage."

In view of these many and diverse needs, patients called for a competitive market of product choices and resented any efforts to cut off that choice. Indeed, they have been attentively studying this very litigation—precisely because its outcome will affect how many treatment choices these patients have and how much they will cost. They are uniformly critical of Jazz's aggressive intellec-

tual property strategy: "We won't even be able to see a once-nightly version of Xywav," one commenter wrote, "for another 15 years or so." And they are thoroughly unimpressed with the theory of the present case, in which Jazz challenges the determination that Lumryz was clinically superior. As one well-received comment said of this case, "Jazz says the once night dose is not beneficial to clients. L[aughing]o[ut]l[oud]."

II. The Orphan Drug Act Is Best Read Not to Treat the Once-Nightly Product as the "Same Drug" as a Twice-Nightly One

Patients' health care needs are important in their own right, but they are also important to the doctrinal question of this case, namely the interpretation of the phrase "same drug" in the ODA. This is because, read in view of congressional intent and legal theory, "same drug" is a scope-setting term that properly entails an inquiry into policy questions of innovation, competition, and patient welfare.

A. In Enacting Orphan Drug Exclusivity, Congress Intentionally Balanced Patient Interests and Innovation Incentives

From its inception, the ODA has placed the interests of patients with rare diseases front and center. The incentive structure of exclusivity under the statute is not a free-floating boon to orphan drug developers, but is limited and tied to patient welfare. To interpret the statute in a manner that deprives patients of critical health benefits, then, would be inconsistent with the text and legislative

intent.

On its face, the ODA makes its patient focus plain. In its congressional findings, the statute lists a number of rare diseases and conditions, and including "Huntington's disease, myoclonus, ALS (Lou Gehrig's disease), Tourette syndrome, and muscular dystrophy," and predicts that "some promising orphan drugs will not be developed" for these rare diseases absent "laws to reduce the costs of developing such drugs and to provide financial incentives to develop such drugs." Pub. L. No. 97-414, § 1(b)(1), (5), 96 Stat. 2049, 2049. Accordingly, Congress relied on "the public interest"—particularly the interest in helping patients with rare diseases—to justify drug development incentives. *Id.* § 1(b)(6), 96 Stat. at 2049.

Limitations and exceptions to orphan drug exclusivity confirm that Congress intended to balance incentives in favor of patients. Exclusivity is limited to seven years, and can be revoked if the exclusivity holder "cannot ensure the availability of sufficient quantities of the drug to meet the needs of persons with the disease or condition" for which the exclusivity was granted. 21 U.S.C. § 360cc(b)(1); *see also Orphan Drug Amendments of 1985*, H.R. Rep. No. 99-153, at 5–6 (1985) (noting importance of limitations to orphan drug exclusivity); 131 Cong. Rec. 15864 (same). These limitations mean that orphan drug exclusivity "does not produce so sweeping a monopoly" over a designated drug. *Baker Norton Pharms., Inc. v.*

U.S. Food & Drug Admin., 132 F. Supp. 2d 30, 37 (D.D.C. 2001).

Amendments to the statute in 2017 further advance the statute's balancing between patient interests and financial incentives. Three years prior, *Depomed, Inc. v. United States Department of Health & Human Services* had held that orphan drug exclusivity could (and, indeed, was required to) be granted on an old and previously approved drug, relying on a view that "the statute plainly incentivizes investment in drugs" through the grant of exclusivity. 66 F. Supp. 3d 217, 235 (D.D.C. 2014). Congress moved swiftly to abrogate this result, prohibiting orphan drug exclusivity on previously approved drugs absent a showing of clinical superiority. FDA Reauthorization Act of 2017, Pub. L. No. 115-52, sec. 607(a)(3), 131 Stat. 1005, 1049 (codified at 21 U.S.C. § 360cc(c)(1)). In explaining the amendment, Rep. Walters observed that it would "limit the number of drugs that are automatically entitled to seven years of exclusivity, while maintaining incentives for the development of innovative treatments for rare diseases." 163 Cong. Rec. H5483 (July 12, 2017). The 2017 amendments thus rejected the incentives-only view of *Depomed*, preferring instead a limited exclusivity that favored orphan drugs offering "greater efficacy, greater safety, or . . . a major contribution to patient care." 21 U.S.C. § 360cc(c)(2).

Given this statutory language and legislative history, patient interests have weighed heavily in the eyes of courts interpreting the ODA, including the mean-

ing of "same drug." *See, e.g., Genentech, Inc. v. Bowen*, 676 F. Supp. 301, 312 (D.D.C. 1987) ("The legislative history is replete with references to the fundamental need to provide treatment for presently untreated patients . . . ."); *Baker Norton*, 132 F. Supp. 2d at 38 (relying on the "interests of patients who need such drugs" as part of "the obvious legislative intent"); *Spectrum Pharms., Inc. v. Burwell*, 824 F.3d 1062, 1067 (D.C. Cir. 2016) ("[I]nnovation was not Congress's only concern . . . . Congress also sought to promote *affordable* drugs."); *Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 147 (4th Cir. 2002) (interpreting the ODA "[i]n light of the ensuing effects on the delivery of health care and drug prices in this country").

B. The Scope of Orphan Drug Exclusivity, Embodied in the Phrase "Same Drug," Implements This Balance

Interpretation of the statutory phrase "same drug" in this case critically affects the patient welfare interests that the ODA is meant to serve. This is because "same drug" defines the *scope* of orphan drug exclusivity: the breadth of similar products that the exclusivity holder can keep off the market. *Depomed*, 66 F. Supp. 3d at 232; *see also Genentech*, 676 F. at 312 (applying "broad policy objectives" to interpret the word "drug"). While too narrow a scope of exclusivity could undermine incentives for drug development, too broad a scope would keep valuable improved drugs off the market to the detriment of patient interests. *See Baker Norton*, 132 F. Supp. 2d at 38. Correctly setting the scope of exclusivity in view

of the phrase "same drug" is thus essential for the statute to achieve its intended purposes.

While the authorities on orphan drug exclusivity provide some guidance as to the ramifications of scope, a useful comparator may be found in another regime of market exclusivity: patent law. The ODA has long been influenced by patent law, *see, e.g.,* H.R. Rep. No. 99-153, *supra*, at 3–4, and the overall structure of the exclusivities is strikingly similar. Like the ODA, patent law grants to the inventor of a new technology a time-limited exclusivity over a defined scope of products or activities relating to the patented invention. *See* 35 U.S.C. § 154(a)(2) (patent term); § 271(a) (infringement). More importantly, patent law entails the same balancing between the public interest and innovation incentives as the ODA. Patents are often characterized as a "carefully crafted bargain" in which the public grants temporary exclusivity over inventions as an incentive for inventors to make new technologies available to the public. *E.g., Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150–51 (1989). "[T]he limited and temporary monopoly granted to inventors was never designed for their exclusive profit or advantage; the benefit to the public or community at large was another and doubtless the primary object in granting and securing that monopoly." *Kendall v. Winsor*, 62 U.S. (21 How.) 322, 327–28 (1859).

Given its similarities to the ODA, patent law can offer guidance on how the

scope of an exclusivity affects objectives like patient welfare.[4] In particular, patent jurisprudence and theory offer two specific pitfalls of overbroad scope of exclusivity, pitfalls that can directly inform how this Court should interpret "same drug."

1. Overbroad Scope Discourages Welfare-Enhancing Competition

The first pitfall of excessive scope is harm to competition. Competitors in a market have incentives to improve their products and grab market share, but an exclusivity covering too wide a range of products or services blocks and discourages that innovative, consumer-beneficial technology. *See* Fed. Trade Comm'n, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy* ch. 1, at 11–12 (2003), *available online*; *Eon-Net LP v. Flagstar Bancorp*, 653 F.3d 1314, 1326–28 (Fed. Cir. 2011) (observing harms of vexatious litigation arising out of an improperly broad patent on electronic communications). "When a broad patent is granted," two legal commentators write, "its scope diminishes

[4]Certainly, the alignment between patents and orphan drug exclusivity is not perfect. In particular, patentability determinations do not implicate *Chevron* deference, and patents can operate to exclude superior products. But patent law has other tools for maintaining the balance of scope, such as claim construction. *See* Tun-Jen Chiang & Lawrence B. Solum, *The Interpretation–Construction Distinction in Patent Law*, 123 Yale L.J. 530, 536–37 (2013); Peter Lee, *Substantive Claim Construction as a Patent Scope Lever*, 1 IP Theory 100 (2010). Accordingly, it would be improper for the Court simply to import the mechanics of patent law into the ODA; it should instead focus on the underlying principles and motivations.

incentives for others to stay in the invention game." Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 Colum. L. Rev. 839, 916 (1990). And without those others remaining in the invention game, patients and consumers do not receive the benefits of those others' inventive efforts.

Because overbroad patents can impair competition and diminish development of publicly beneficial new technologies, the Supreme Court has repeatedly warned that "the 'public' also has a 'paramount interest in seeing that patent monopolies . . . are kept within their legitimate scope.' " *Medtronic, Inc. v. Mirowski Family Ventures, LLC*, 571 U.S. 191, 203 (2014) (quoting *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 816 (1945)); *see also Lear, Inc. v. Adkins*, 395 U.S. 653, 664 (1969) ("It is [] important to the public that competition should not be repressed . . . .") (quoting *Pope Mfg. Co. v. Gormully*, 144 U.S. 224, 234 (1892)); *Blonder-Tongue Lab'ys, Inc. v. Univ. of Ill. Found.*, 402 U.S. 313, 349–50 (1971) ("[T]he holder of a patent should not be . . . allowed to exact royalties for the use of an idea . . . that is beyond the scope of the patent monopoly granted . . . .").

That harm is precisely at issue in this case: Competition spurs companies like Avadel to develop products like Lumryz that are superior to the incumbents. Should Jazz's orphan drug exclusivity be given such broad scope as to exclude superior improvements, the impairment to competition will diminish patient welfare.

2. Overbroad Scope Creates an "Innovation Disincentive"

The second pitfall is more complex but also more pernicious: Overbroad exclusivity scope can create an *innovation disincentive* in which the exclusivity holder lacks motivation to make useful improvements. Some basic economics of patents can explain this bizarre yet surprisingly common situation. Ordinarily, exclusivities like patents cover a specific product, leaving consumers free to choose substitutes outside the scope of the exclusivity. *See* Fed. Trade Comm'n, *supra*, at 8; *Ill. Tool Works Inc. v. Indep. Ink, Inc.*, 547 U.S. 28, 45 (2006). As a result, the exclusivity is only valuable if the covered product is a major improvement. *See, e.g.*, Daniel J. Hemel & Lisa Larrimore Ouellette, *Innovation Policy Pluralism*, 128 Yale L.J. 544, 548 (2019). For example, in a properly functioning market, one would expect asthma patients to pay brand-name prices for a patented new inhaler only if it works much better than old, low-cost generics. Inhaler manufacturers should thus theoretically invest only in developing substantially better inhalers, since minor improvements ought to gain little market traction. A properly scoped patent exclusivity, in tandem with "the baseline of free competition," is the basis for the incentive to invent. *See Bonito Boats*, 489 U.S. at 156.

But what if a patent's scope is so broad that other competitors are kicked out of the market and consumers have only the patented product to choose? This market-dominant patent holder has little incentive to improve its products, as it

already extracts all available profit through monopoly pricing and has no more market share to build through improvements. *See* Charles Duan, *Mandatory Infringement*, 75 Fla. L. Rev. 219, 255–58 (2023). An asthma inhaler company wielding market power through patents might invest in trivially beneficial improvements, knowing that asthmatics will pay top dollar regardless of how good the inhaler is. *See* Oliver J. Wouters et al., *Product Hopping in the Drug Industry—Lessons from Albuterol*, 387 New Eng. J. Med. 1153 (2022); Erik R. Swenson, *The True Environmental Cost of Chlorofluorocarbon-Based Inhalers*, 175 JAMA Internal Med. 1867, 1867 (2015); Anupam B. Jena et al., *The Impact of the US Food and Drug Administration Chlorofluorocarbon Ban on Out-of-Pocket Costs and Use of Albuterol Inhalers Among Individuals with Asthma*, 175 JAMA Internal Med. 1171, 1176 (2015); *see also* Bernard Chao, *Horizontal Innovation and Interface Patents*, 2016 Wis. L. Rev. 287, 295–96. In numerous industries including pharmaceuticals, safety standards, and textbooks, the innovation disincentive effect of too-broad exclusivity scope is easily found. *See* Duan, *supra*, at 255–58.

At best, an exclusivity holder will have an incentive to introduce marginal improvements just before its exclusivity expires, and render its old product unobtainable or undesirable right before competition begins. This so-called "product-hopping" strategy that has been roundly criticized in antitrust and consumer protection circles. *See, e.g.,* Michael A. Carrier & Steve D. Shadowen, *Product*

Hopping: A New Framework, 92 Notre Dame L. Rev. 167 (2016); Daniel Burke, *An Examination of Product Hopping by Brand-Name Prescription Drug Manufacturers: The Problem and a Proposed Solution*, 66 Clev. State L. Rev. 415 (2018); Alex Brill, Matrix Glob. Advisors, *The Cost of Brand Drug Product Hopping* (Sept. 2020), *available online*; Markus H. Meier et al., Fed. Trade Comm'n, *Overview of FTC Actions in Pharmaceutical Products and Distribution* 83–84 (June 2019), *available online*. Particularly relevant here, a common product-hopping practice is to make simple tweaks to inactive components of a drug—swapping out sodium for another salt, for example, as Jazz has done with its Xywav product. *See* Steve D. Shadowen et al., *Anticompetitive Product Changes in the Pharmaceutical Industry*, 41 Rutgers L.J. 1, 25 (2009). Such changes are typically easy to make, and often have little patient benefit. *See id.* at 33–35 & tbl.4.

The innovation disincentive problem has already arisen in a different aspect of the ODA. Recently in *Catalyst Pharmaceuticals, Inc. v. Becerra*, the pharmaceutical company Catalyst held an orphan drug exclusivity on the drug amifampridine to treat Lambert-Eaton Myasthenic Syndrome ("LEMS"), and another company Jacobus sought approval for pediatric use of amifampridine (for which Catalyst's product was not approved). *See* 14 F.4th 1299, 1304 (11th Cir. 2021). The FDA approved Jacobus's product in view of the different population it served, but the Eleventh Circuit held that approval in error. Focusing on language of the

ODA that granted exclusivity over "the same drug *for the same disease or condition*," the court held that the scope of the exclusivity covered all LEMS patients, pediatric or not. *See Catalyst*, 14 F.4th at 1311–12.

But that left children with LEMS in the cold: Catalyst's product was not approved for them, and Jacobus's was barred by exclusivity. As a result, as observed in a letter signed by over eighty patient organizations, the decision "would incentivize sponsors to seek broader designations for an entire rare disease at the outset, leaving little incentive to continue to study the safety and efficacy of that drug in special populations, like children." Letter from Nat'l Org. for Rare Disorders et al. to Patty Murray & Richard Burr, Comm. on Health, Educ., Lab. & Pensions, U.S. Senate 2 (June 3, 2022), *available online*. The FDA similarly expressed concern with *Catalyst*, concluding that a narrower view of orphan drug exclusivity scope would better "incentivize sponsors to continue to develop a drug for use in all persons affected by a rare disease or condition." Clarification of Orphan-Drug Exclusivity Following Catalyst Pharms., Inc. v. Becerra, 88 Fed. Reg. 4086, 4087 (Food & Drug Admin. Jan. 24, 2023). The Eleventh Circuit's decision on orphan drug exclusivity scope, these commentators said, was closely tied to reduced competition, innovation disincentives, and ultimately harms to patients with rare diseases.

C. The FDA's Current Interpretation of "Same Drug" Better Serves Patient Welfare, Competition, and Innovation

The implications of orphan drug exclusivity scope for competition and patient welfare weigh in favor of the FDA's interpretation of "same drug," and in particular the clinical superiority exception.

Initially, the technical and scientific expertise of the FDA positions the agency well to assess the proper scope of orphan drug exclusivity. Balancing the interests of competition, innovation, and patient welfare is a complex exercise, for which the agency's views ought to be highly informative. *See Spectrum*, 824 F.3d at 1068. The FDA's history of rulemaking on the ODA reflects the agency's willingness to engage in this balancing exercise. Furthermore, the statutory text and legislative history of the ODA suggest that Congress intended that innovation and patient interests be balanced in the interpretation of the statute. *See Baker Norton*, 132 F. Supp. 2d at 36.

And the determination that the agency reached in this case is consistent with the plain and ordinary meaning of "same drug." *See, e.g., Wooden v. United States*, 142 S. Ct. 1063, 1069 (2022); *New Prime, Inc. v. Oliveira*, 139 S. Ct. 532, 539 (2019). A drug taken on a different dosing schedule that presents major benefits to patients is plainly not the "same." Furthermore, insofar as the purpose of exclusivity the statute is to prevent competitors simply from free-riding on an orphan drug approval, a clinically superior product that requires its own trials and approval

does not present that free-riding concern.

This Court should maintain the clinical superiority exception in interpreting the phrase "same drug." The exception mitigates the innovation disincentive problem. If competitors like Avadel can introduce improved, clinically superior oxybate products that win patients over and capture substantial market share, then exclusivity-holding incumbents will have to keep innovating and developing better products to keep pace. Certainly Jazz is entitled to exclusivity over the twice-nightly product that it commercialized, but patients and society are best served by a steady stream of improvements to drugs rather than the innovation disincentive of broad exclusivity scope. Deeming a clinically superior drug not the "same drug" best serves those interests.

The clinical superiority exception should be broadly viewed in view of the diversity of patients and reactions to the drugs at issue. Jazz calls on this Court to adopt a rigid rule that a new product cannot be clinically superior if it lacks an unrelated improvement such as lower sodium content. Perhaps such a rule might be tenable if every patient was uniformly harmed by sodium, but they are not. Many patients felt unaffected by sodium content, others disliked Xywav for separate reasons such as its inclusion of artificial sweeteners, and still others were happy to accept higher sodium for sleeping through the night.

What is important to narcolepsy patients here is having a variety of choices

available to them—in particular, the choice not to settle for the tribulations of twice-nightly dosing. The clinical superiority exception and the "same drug" statutory language can accommodate this patient need for choice, and thereby satisfies important interests of innovation, competition, and patient welfare.

CONCLUSION

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

Respectfully submitted,

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