No. 23-768

IN THE

Supreme Court of the United States

VANDA PHARMACEUTICALS INC.,
Petitioner,
v.
TEVA PHARMACEUTICALS USA, INC.;
APOTEX INC.; APOTEX CORP.,
Respondents.

ON PETITION FOR WRIT OF CERTIORARI TO
THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

BRIEF OF THE AMERICAN COUNCIL OF THE BLIND, BLINDED VETERANS ASSOCIATION, AND PRISMS AS AMICI CURIAE IN SUPPORT OF PETITIONER

Jeffrey T. Quilici
ORRICK, HERRINGTON &
SUTCLIFFE LLP
300 W. 6th Street
Suite 1850
Austin, TX 78701

Mark S. Davies
Counsel of Record
ORRICK, HERRINGTON &
SUTCLIFFE LLP
1152 15th Street, NW
Washington, DC 20005
(202) 339-8400
mark.davies@orrick.com

Counsel for Amici Curiae

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INTEREST OF AMICI CURIAE[1]

The American Council of the Blind (ACB) is a national nonprofit, consumer organization of the blind, striving to increase the quality of life for all people who are blind and visually impaired by working to increase their independence, security, and equality of opportunity. Throughout its history, the ACB has advocated for the interests of the blind and visually impaired in Congress and the courts. ACB believes that the Federal Circuit's decision in this case jeopardizes this mission.

ACB has seventy state chapters and affiliates and thousands of individual members in all fifty states. Among those individual members are many who suffer from Non-24 Hour Sleep-Wake Disorder (Non-24), a debilitating condition cyclic circadian rhythm sleep disorder characterized by an inability to sleep on a 24-hour schedule. ACB members report that Hetlioz®, the patented drug at issue in this litigation, is the most effective treatment for Non-24.

The Blinded Veterans Association (BVA) is the only national veterans' organization congressionally chartered and exclusively dedicated to blinded veterans and their families. BVA seeks to assist all veterans and their families coping with sight loss, through a combination of expert advocacy, engaged member-

[1] No counsel for a party authored the brief in whole or in part. No party, counsel for a party, or any person other than amici and their counsel made a monetary contribution intended to fund the preparation or submission of the brief.

ship, clear communication and peer inspired self-reliance. BVA members affected by Non-24 similarly report that Hetlioz® has markedly improved their lives.

PRISMS (Parents & Researchers Interested in Smith-Magenis Syndrome) is a nonprofit charitable organization dedicated to providing information and support to families of persons suffering from Smith-Magenis syndrome (SMS). SMS is a rare chromosomal disorder caused by an absence of certain genetic material from a specific region of chromosome 17, and is characterized by a specific pattern of physical, behavioral, and developmental features, including in many cases sleep disorders. Organized in 1993, PRISMS sponsors research and fosters partnerships with companies and professionals to increase awareness and understanding of SMS. PRISMS also encourages, inspires and supports researchers to encourage developments of treatments for the disorder and improve the lives of everyone affected by SMS. PRISMS was involved in recruiting test subjects for clinical studies of Hetlioz® and advocated alongside plaintiff Vanda for approval of Hetlioz® for the treatment of SMS-related sleep disorders before the Food and Drug Administration (FDA).

Amici believe this case is highly important to blind and visually impaired persons, including veterans, as well as SMS patients across the United States. These populations are small relative to the population as a whole, and historically have been underserved by the pharmaceutical industry as a result. The life experiences of Jerry Berrier, Suzanne Erb, and Debbie Grubb discussed below illustrate the importance of encouraging development of drugs for such small and

underserved patient populations. They also highlight results that the Federal Circuit's decision endangers by undermining the crucial role that patent incentives play in the development of such treatments. Amici urge this Court to grant the petition for certiorari and reverse the judgment below.

INTRODUCTION AND SUMMARY OF ARGUMENT

Amici submit this brief to highlight the dangerous life-altering consequences of the Federal Circuit's decision below. All companies pioneering new medicines face practical and economic challenges, but those challenges are particularly acute for medicines that target rare disease states like Non-24 and SMS-related sleep disorders, each of which affects only a few tens of thousands of patients in the United States. Petitioner Vanda Pharmaceuticals Inc. navigated the practical and economic hurdles of serving these modest populations to develop Hetlioz®, the most effective treatment yet available for Non-24 and SMS-related sleep disorders.

That navigation is one we should encourage. As the patients themselves report below, the results of Vanda's new treatment were dramatic, giving them back something most of us usually take for granted: the ability to sleep at night and stay awake during the day. But the decision below instead undermines the incentives for pharmaceutical companies to follow Vanda's course in the future.

Companies must pick and choose which treatments to research, and part of that calculation is economic. A candidate medication, however promising, may be passed over if there is simply no way to recover the costs of developing it. Patent protections help ensure that the company will indeed have a time of market exclusivity in which to do so.

Under the Federal Circuit's incorrect standard for obviousness, every company faces a higher risk that the treatment it considers developing today may be quickly overtaken by generic versions after approval That distortion of the carefully calibrated incentives provided by the Patent Act and this Court's case law will inevitably lead to fewer treatments being developed for small and underserved patient populations across the United States.

The Court should grant review of the Federal Circuit's decision because of the substantial harm it would inflict on medically-needy yet modestly-sized communities across the United States.

ARGUMENT

I. New drugs for underserved patient populations make meaningful differences in patients' lives.

The many tragedies avoided by the discovery of tasimelteon as a treatment for Non-24 and SMS are poignantly illustrated by the stories of those whose lives have been changed by Hetlioz®.

Each patient with whom counsel has spoken brings his or her own story of the hardships of living with Non-24, the failed attempts to find a solution, and the profound impact of finally finding a treatment that actually worked. While Amici could relate many such stories, they will instead focus on three.

* * *

Jerry Berrier was born in 1952, with retinopathy. He recalls being able to perceive light during his childhood, but in his teenage years he lost even that. At the age of 18, he developed "horrible sleeping problems" that would come and go in a cyclical rhythm. For a time, he would be able to get a normal night's rest. A week or two later, he would get at most a scant few hours. And shortly thereafter, he would be completely unable to sleep at night, before returning to the top of the cycle.

This on-again, off-again existence deeply affected his college experience. "I don't know how I got through," he says. And it continued throughout most of his working years as an employment interviewer. While he "managed not to miss work" most of the time, it was nevertheless "pretty miserable. Sometimes, I was going to work on 45 minutes of sleep. Sometimes none."

And nothing he tried seemed to help. As many Non-24 patients do, Jerry experimented with over-the-counter melatonin, but found that it quickly—and apparently permanently—ceased to have much effect on his sleep. Caffeine only masked the symptoms. And

prescription sleep aids such as Ambien quickly produced severe side effects.

Hetlioz® changed everything for Jerry. He learned about it through a study conducted at Brigham & Women's Hospital in Boston. Although he could never be certain whether he was getting the medicine or a placebo, "it seemed to help." While he was "taking a capsule every night," his sleep quickly became more consistent. After that highly encouraging experience, he sought out Hetlioz® as soon as it became available on the market. "I still don't always get as much sleep as I want, but I nearly always get at least 5 hours a night. And there are no bad side effects." For the first time, Jerry was able to rely on sleeping and being able to function the next day, rather than simply hope.

* * *

Suzanne Erb "has had Non-24 as long as I can remember." At the age of 7 or 8, she lost her eyes, and any light perception with them. Quickly, she started "being awake all night," and remembers routinely seeing all the wee hours of the clock as an elementary school student. And her condition, like Jerry's, continued through college and her working life.

She "called it rock-around-the-clock syndrome" because her sleep schedule would cycle from four or five hours a night, to only two, to none, and back again. "I would feel like night should be day and day should be night. It was like constant jet lag." And while she describes drinking "huge amounts of coffee

as self-medication," she would suffer terrible migraines. "I could never take vacation days. I had to use them for sick days instead." Non-24, she notes, affects all aspects of her life; chronic sleeplessness "can determine how you respond to things. Your reaction time. Even your ability to remember to follow through on things." In Suzanne's view, living with Non-24 "can be more debilitating at times than blindness."

Suzanne also had little success with other treatments. Melatonin "didn't do the job," she recalls. And neither antidepressants nor sleeping aids seemed to solve the problem. Taking Hetlioz®, however, "has been like day and night for me. Pun very much intended." She first started the medication during the clinical trials more than ten years ago, and realized within a handful of days that she was not on the placebo. "I slept better than I had in maybe 50 years. And I had so much energy. Not pumped up from caffeine; just from me." Since that time, she has been consistently getting 4-5 hours of sleep a night. "That's actually a big deal. I still have Non-24, and I will always have Non-24. But I'm so much more able to live a stable life." Thinking back on her long years of sleeplessness, she mused "If I'd had access to something like Hetlioz® in my 20s, I'd probably have a Ph.D."

* * *

Debbie Grubb also "fought Non-24 all the way" throughout her life. "I would be lying there in bed, tossing and turning, praying for sleep" but not finding any. "I knew what the next day would bring," she says. Though she describes herself as a "busy-bee per-

son" who would buckle down and get through workdays regardless, every time she was "wide awake all night," she would "have this dreadful sleepiness during the days. I would have to dig in my toes just so that I wouldn't drift off to sleep."

Debbie found it hard to explain to others why living with Non-24 was "such a debilitating thing." "Many people," she says, "just think you should take melatonin, or a sleeping medication, and that should fix it. But they don't work. They don't fix your circadian rhythm clock, and people need to understand that."

Debbie, too, heard about Vanda's treatment for Non-24 while it was still in development. "I participated in the clinical trials for months." And Hetlioz® "made a big, big difference" in her life. Most nights, she says, she sleeps very soundly, and almost always at least 4-6 hours. To be sure, she reports having the occasional night when "I don't sleep as well. But everyone has those." For more than ten years, she has felt "wonderful knowing I can go to bed and actually sleep" with no side effects.

Debbie also made a point of expressing her gratitude to the company that chose to tackle her condition. "I'm not usually pro-big-business," Debbie says, and she understands why generic medications exist. But she insisted that it was only right to protect "companies that go out on a limb, the ones that make drugs for a very small target population." Vanda, she says, is one of those companies. "And it's going to limit them, limit many companies, when they can't realize

the full financial benefit from the drugs that they are making."

* * *

These stories have many things in common with each other and with many untold stories of other Non-24 and SMS patients who have found respite from their condition through this new treatment. Each of them suffered terribly from a rare but debilitating sleep disorder. Each of them bravely soldiered on for decades of their adult lives in which no treatment was available and effective. And each of them has taken a dramatic turn for the better since Hetlioz® came on the market and gave them back a measure of control over their sleep cycles, and, with that, their waking lives.

But the most important commonality may be this: each of them recovered that control because one company took a risk. Vanda could have investigated treatments for a host of conditions, most of which are far more common in the United States. A new and improved medication for cancer or heart disease, for example, would immediately gain millions of customers. Vanda instead chose to research treatments for a small population—in this country, mere tens of thousands—that had gone decades with little hope for relief.

If we want the next pharmaceutical company to tackle the next such problem, to take on the costs and risks of seeking a cure for the next "debilitating" but only narrowly-spread condition, we cannot undercut their financial incentive to do so. But as discussed

next, the Federal Circuit's decision below does just that, by weakening the patent protections that pharmaceutical companies rely on when choosing their research paths.

II. Weakening patent protection undermines the incentives that support development of new drugs for underserved patient populations.

Properly calibrated patent protection is crucial to provide the incentive needed to undertake enormously expensive research and development of new medicines. This is doubly true for medicines that target disease states with small patient populations. Indeed, had the Federal Circuit's decision below been in place when Vanda considered whether to investigate tasimelteon as a treatment for Non-24 and SMS, Hetlioz® might never have been developed.

Non-24 and SMS-related sleep disorders do not affect many. For example, Non-24 is estimated to affect at least 50% of blind people who lack any light perception at all. Roneil G. Malkani et al., *Diagnostic and Treatment Challenges of Sighted Non–24-Hour Sleep-Wake Disorder*, 14 J. Clin. Sleep Med. 603, 603 (2018); *see also* Maria Antonia Quera Salva et al., *Non-24- Hour Sleep–Wake Rhythm Disorder in the Totally Blind: Diagnosis and Management,* 8 Front. Neurol., art. 686, 4 (2017), http://tinyurl.com/4938zj2h. But it is rare among sighted individuals. Malkani, *supra*, at 603. Thus, Non-24 is estimated to affect only 65,000 to 95,000 people in the U.S. Annie Daly & Valerie Coppenrath, *Non-24-Hour*

Sleep-Wake Disorder: Disease Overview and Treatment Options, U.S. Pharmacist (2015) 48, http://tinyurl.com/34swc7x9. SMS-related sleep disorders are similarly rare; NIH estimates fewer than 50,000 U.S. patients suffer from SMS. Nat'l Insts. of Health, *Smith-Magenis Syndrome* (last updated Jan. 2024), http://tinyurl.com/595y7bbs.

Yet bringing any new drug to market is undeniably expensive. More than two decades ago, academics reported that "it takes several hundred million dollars to discover, develop, and gain regulatory approval for a new medicine." Henry Grabowski, *Patents, Innovation and Access to New Pharmaceuticals*, 5 J. Int'l Econ. L. 849, 851 (2002) (hereinafter "Grabowski, *Patents*"). A more recent academic survey found estimates of research and development costs per drug ranging from hundreds of millions of dollars to several billion, Stephanie Rennane et al., *Estimating the Cost of Industry Investment in Drug Research and Development: A Review of Methods and Results*, 58 INQUIRY: The Journal of Health Care Organization, Provision, and Financing 1, 3 (2021). And the Congressional Budget Office reports estimates for the total development cost of a new drug "rang[ing] from less than $1 billion to more than $2 billion." Congressional Budget Office, *Research and Development in the Pharmaceutical Industry* 2 (Apr. 2021), http://tinyurl.com/2wash4hv (hereinafter "CBO"). Not only are these costs enormous, so is the time required. One industry group, Biotechnology Innovation Organization (BIO), analyzed over 9700 clinical development programs over the course of a decade and found that it takes an average of 10.5 years to progress from a Phase I clinical trial to regulatory approval. David

Thomas et al., *Clinical Development Success Rates and Contributing Factors 2011-2020*, BIO 3, 24 (Feb. 2021) (hereinafter "Thomas 2021"); *see also* CBO, *supra*, at 14.

In part, these high costs are driven by the uncertainty inherent in pioneering new medicines. Pharmaceutical companies investigate and develop many drug candidates that never even enter clinical trials. CBO, *supra*, at 14; Grabowski, *Patents*, *supra*, at 851 ("Typically, fewer than 1% of the compounds examined in the pre-clinical period make it into human testing."). And of those few that do, fewer than one in seven—and by many estimates, far fewer—will result in even a single sale to the public. CBO, *supra*, at 13-14 ("recent estimates" of the fraction of drugs in clinical trial that will reach the market "range from 10 percent to 14 percent" and average 12%); *see also* Chi Heem Wong et al., *Estimation of clinical trial success rates and related parameters*, 20 Biostatistics 273, 277 (2019) (13.8% of all drug development programs lead to approval, and as low as 3.4% in oncology); David Thomas et al., *Clinical Development Success Rates 2006-2015*, BIO 7, 11 (2016), https://tinyurl.com/y2n8rnzb (hereinafter "Thomas 2016") (9.6% approval rate for candidates in Phase I trials). Thus, pharmaceutical companies must "initiate drug projects knowing that most of them will not yield a marketable drug." CBO, *supra*, at 13.

Why would pharmaceutical companies undertake such enormous risks over so many years? They must hope to recoup their investments through later sales of the handful of candidates that succeed.

But generic drug makers present a challenge to that model. After one pharmaceutical company has discovered a new therapy, proved its efficacy and safety through years of trials, and won approval from the FDA, a generic manufacturer can win FDA approval and enter the market by relying on the studies and other work already undertaken.

With their dramatically lower costs of entry, generic manufacturers can afford to charge correspondingly lower prices for their medicines. As a result, "generic drugs tend to rapidly supplant sales of the corresponding brand-name drug following generic entry." Henry Grabowski et al., *Recent trends in brand-name and generic drug competition*, 17 J. Med. Econ. 207, 208 (2014) (hereinafter "Grabowski, *Trends*"). That effect has only increased over time. In 2000, brand-name manufacturers could expect to retain around 44% market share one year after the first generic entered the market, but that figure fell to only 16% by 2012. *Id.* at 212-13 & Fig. 4. Thus, without some way to postpone the entry of generic competitors, pharmaceutical companies would face both market-share and price erosion, making it much harder to recover their R&D expenses.

Patent protection is therefore a key counterweight that helps make pharmaceutical development economically viable. By patenting its novel treatment, a brand-name manufacturer can ensure that it has a sufficiently long period of time of exclusive sales in

the market in which to recoup its costs.[2] But without that period of exclusivity, a brand-name manufacturer would only be able to undertake development of treatments that would recoup their development costs extremely quickly, before generic manufacturers imitate its products, erode its prices, and divide its market share.

The ability to obtain a patent can therefore represent a make-or-break decision point in a company's research plan. If a company can be confident of obtaining a patent on a promising treatment candidate, it will be more willing to undertake the immense investment required to develop that treatment; if it cannot, it will seek to invest its money elsewhere. *See, e.g.*, Heidi L. Williams, *How Do Patents Affect Research Investments?*, 9 Annu. Rev. Econ. 441, 450 (2017) (in "a few industries—namely, chemicals and pharmaceuticals—firms report that patents are essential for spurring R&D investments").

The Federal Circuit's decision below fundamentally undermines that confidence. In relying on a company's willingness to undertake clinical trials—a necessary part of developing a new medicine—as a reason to *invalidate* a patent, the decision below necessarily makes it less likely that any treatment a company considers developing today will enjoy patent protection when it comes time to recover the cost of

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[2] While some drug developers may elect instead to license their patents to manufacturers, the economic calculus remains largely the same: because the patent provides the developer the right to exclude other manufacturers, it can obtain license fees from the entire potential market for the products they develop.

that development. *See* Pet. e.g., 13, 20, 30. That risk of loss will inevitably lead some pharmaceutical companies to turn away from developing some treatments, simply because the risk of losing their investments is now much higher than it should be. Medicines that could and should have changed patients' lives will never be pursued.

The importance of well-calibrated patent protection is redoubled in the case of disease states that affect discrete, small populations. Where a disease state affects only a relatively small population, a company contemplating whether to investigate and develop a treatment for the condition cannot rely on large sales volume to recover its investment quickly. Unless the Federal Circuit's opinion is reversed, we may never know what treatments would have existed tomorrow, but now never will.

CONCLUSION

This Court should grant the petition for certiorari.

Respectfully submitted,

Jeffrey T. Quilici
ORRICK, HERRINGTON & SUTCLIFFE LLP
300 W. 6th Street
Suite 1850
Austin, TX 78701

Mark S. Davies
Counsel of Record
ORRICK, HERRINGTON & SUTCLIFFE LLP
1152 15th Street, NW
Washington, DC 20005
(202) 339-8400
mark.davies@orrick.com

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