NO. 20-1119

In the
Supreme Court of the United States

AMARIN PHARMA, INC. and
AMARIN PHARMACEUTICALS IRELAND LIMITED,
Petitioners,

v.

HIKMA PHARMACEUTICALS USA INC.,
HIKMA PHARMACEUTICALS INTERNATIONAL LIMITED,
DR. REDDY'S LABORATORIES, INC. and
DR. REDDY'S LABORATORIES, LTD.,
Respondents.

On Petition for Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

BRIEF FOR *AMICUS CURIAE* AIMED ALLIANCE IN SUPPORT OF PETITIONERS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Other Authorities

STATEMENT OF INTEREST[1]

Aimed Alliance is a not-for-profit health-policy organization that works to protect and enhance the rights of health-care consumers and providers. Aimed Alliance advances its mission by engaging in activities that help patients gain access to medical treatments and care, including by educating patients on their legal rights and their available treatment options. Among its policy priorities, Aimed Alliance focuses on the importance of value and innovation in helping patients gain access to the medications they need. Aimed Alliance assists patients with complex, chronic, and debilitating conditions, including patients who suffer from cardiovascular diseases and severe hypertriglyceridemia.

As part of its efforts to achieve meaningful improvements to the country's health-care system, Aimed Alliance collaborates with a diverse range of health-care stakeholders, including patient advocacy organizations, industry groups, state and federal governments, and charitable foundations. Amarin Corporation plc, the parent to petitioners Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited, is one of those stakeholders.

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[1] As directed by Supreme Court Rule 37.6, *amicus curiae* states that no counsel for any party authored this brief in whole or in part and that no entity or person, aside from *amicus curiae*, its members, and its counsel, made any monetary contribution toward the preparation or submission of this brief. In compliance with Supreme Court Rule 37.2(a), counsel of record for all parties have consented to this filing via email correspondence.

Aimed Alliance is familiar with Amarin's Vascepa® product and the significant benefits it provides to patients with severe hypertriglyceridemia, as well as to patients with elevated triglycerides levels who are on statin therapy. Because Vascepa® meets important, unmet needs for treating such patients, Aimed Alliance submitted comments to the U.S. Food & Drug Administration ("FDA") in November 2019, urging the agency to approve Amarin's supplemental new drug application. It also testified before FDA's Endocrinologic and Metabolic Drugs Advisory Committee. In addition, in August 2019, Aimed Alliance submitted a comment to the Institute of Clinical and Economic Review ("ICER") in response to its "Additive Therapies for Cardiovascular Disease: Effectiveness and Value Draft Evidence Report," because ICER sought feedback on its value-based assessment of Vascepa®.

Drawing on its substantial experience and knowledge in this area, Aimed Alliance offers an important, patient-focused perspective on the issues presented by Amarin's petition. Aimed Alliance submits this amicus brief in hopes that it will aid the Court in understanding the distressing ramifications of the Federal Circuit's approach to evaluating when a patented invention is obvious. In urging the Court to grant certiorari, Aimed Alliance also offers its views on why this case raises an issue of extraordinary, far-reaching importance.

SUMMARY OF ARGUMENT

Ensuring that manufacturers have proper incentives to develop and market new, safe and effective medicines is one of the cornerstones of drug patent law. In this case, however, the Federal Circuit let stand a district court decision that undermines that important objective by invalidating the patents on a groundbreaking, one-of-a-kind invention for treating patients who suffer from a life-threatening lipid disorder. In finding the patented invention obvious in light of prior art, the lower courts departed from this Court's settled precedents. Instead of requiring the patent challenger to prove obviousness with clear and convincing evidence, the district court applied a growing body of Federal Circuit precedent that, upon a mere *prima facie* showing, shifts the burden of production—and in effect persuasion—onto the patent holder. Because the lower courts applied this improper *prima facie* test, they fell victim to hindsight bias and failed to consider the totality of the evidence, including objective evidence that Amarin's invention was a significant advancement over the prior art.

Without this Court's intervention, the Federal Circuit's approach will undermine the incentives that Congress created for individuals and companies to invest in developing innovative medications. The decision below is also expected to reduce the number of patients who are adequately informed about Amarin's innovative therapy, placing those patients at a higher risk for heart attack, stroke, and cardiovascular death. Because this case presents an ideal vehicle for clarifying the standard for evaluating

the obviousness of a patented invention, and because the Federal Circuit's decision reflects that court's entrenched position on what legal test applies, there is no reason to await further developments in the law. The Court should instead grant the petition for certiorari.

ARGUMENT

I. The Federal Circuit's Entrenched Approach to Evaluating Obviousness Calls for Review.

The Federal Circuit's test for obviousness comports with neither the statutory text nor this Court's precedents. In permitting a patent challenger to make a *prima facie* showing of obviousness as a hair-trigger to shifting the burden of proving validity to the patent holder, the Federal Circuit's test erodes the statutory presumption of patent validity. This case offers an ideal vehicle for addressing the Federal Circuit's test and clarifying this important area of federal law.

A. The Federal Circuit's Burden-Shifting Test Violates This Court's Precedents.

The point of the obviousness inquiry is to identify advancements that are so slight or trivial that they would have occurred without the need for patent protection. *See Hotchkiss v. Greenwood*, 52 U.S. 248, 267 (1850) (concluding that a clay doorknob was not entitled to patent protection because the improvement was merely the "work of the skillful mechanic, not that of the inventor"). Section 103 of Title 35 directs that a claim is obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have

been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103. The burden of proving obviousness is supposed to remain at all times with the patent challenger. "[B]y its express terms, [35 U.S.C.] § 282 establishes a presumption of patent validity, and it provides that a challenger must overcome that presumption to prevail on an invalidity defense." *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 100 (2011).

As interpreted by this Court, federal law requires a court asked to invalidate a patent to take account of *all* relevant factors, including objective indicia of non-obviousness. *See Graham v. John Deere Co. of Kan. City*, 383 U.S. 1, 17–18 (1966). The factors bearing on obviousness are to be considered in their totality, weighed together with the burden of persuasion squarely on the patent challenger. *See KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007); *Graham*, 383 U.S. at 17–18. In rejecting the position that a patent challenger is capable of "shifting both the burden of production and the burden of persuasion" to the patentee upon a certain showing, *Microsoft*, 564 U.S. at 103 (internal quotation marks omitted), this Court has affirmed that "a defendant raising an invalidity defense b[ears] 'a heavy burden of persuasion,' requiring proof of the defense by clear and convincing evidence," *id.* at 102 (quoting *Radio Corp. of Am. v. Radio Eng'g Labs.*, 293 U.S. 1, 8 (1934), *as modified on denial of r'hrg* (Oct. 8, 1934)).

Instead of anchoring its analysis to the presumption of validity and a patent challenger's burden to show obviousness clearly and convincingly,

the Federal Circuit's approach relies on an improper burden-shifting framework. Under that approach, as long as the patent challenger makes a *prima facie* showing of obviousness, the burden of production—and in effect persuasion—shifts to the patent holder to prove that secondary considerations refute that *prima facie* showing. *See* App. 81a; *see also* Pet. 26, 29. By shifting the burden and discounting objective indicia of non-obviousness, the Federal Circuit's test raises a particular risk of impermissible hindsight bias. Under the Federal Circuit's approach, patents on even the most novel inventions risk being invalidated when challenged.

B. This Case Presents an Ideal Vehicle for Addressing the Question Presented.

This case presents an ideal vehicle for the Court to clarify the proper standards for determining when a patented invention is obvious. The case brings into sharp focus the serious consequences of the Federal Circuit's burden-shifting approach, which relaxes the standards for demonstrating obviousness. There also can be no doubt that the time is ripe for this Court's intervention. Despite the extraordinary importance of this case, the Federal Circuit views its burden-shifting approach to be so entrenched that it summarily affirmed without even issuing an opinion.

If Amarin's drug is not entitled to patent protection, no drug manufacturer can be confident that its patented inventions will withstand an obviousness defense. Amarin's drug indisputably addresses a previously unmet medical need and took hundreds of millions of dollars to develop. It has been heralded as a "game changer" for patients, Catherine

Hackett, *"Phenomenal" REDUCE-IT Establishes Triglyceride Theory*, MDedge.com (Nov. 20, 2018), and described as a "groundbreaking" drug within the field, *see* Press Release, HLS Therapeutics Inc., HLS Therapeutics Announces Vascepa® (icosapent ethyl) Showed 30% Reduction in Total Cardiovascular Events Including Recurrent Events in REDUCE-IT™ (Mar. 19, 2019). Amarin's drug has received that recognition because, unlike other medications, it has been shown (1) to treat severe hypertriglyceridemia without increasing bad cholesterol and (2) to reduce the risk of major cardiovascular events in statin-treated patients with persistent elevated levels of triglycerides.

Before Amarin's drug, other available treatments for severe hypertriglyceridemia increased bad cholesterol, a major cause of cardiovascular disease. *See* App. 8a (explaining that treatment other than Vascepa® "dramatically increase[d] LDL-C levels"). Amarin's novel solution was to mitigate this harmful tradeoff. *See* Adam Feuerstein, *Amarin Prescription Fish-Oil Pill Approved*, The Street (July 26, 2012). Where others had tried and failed, Amarin's invention demonstrated success. In doing so, it met a "long-felt need for a drug ... that could reduce [triglyceride] levels without raising [bad cholesterol] levels." App. 89a.

Moreover, because the patent system is designed to protect inventions, like Vascepa®, Amarin continued to invest to provide patients with additional innovative benefits. After conducting a clinical trial following more than 8,000 patients for approximately five years, researchers discovered that Amarin's drug

provides significant benefits to patients with persistent elevated triglycerides. Before Vascepa®, heart disease was typically treated with only a single class of drugs, called statins, that acted to reduce bad cholesterol. Vascepa® can be taken in tandem with statins. Compared with a placebo, Vascepa® was shown to reduce the risk of major cardiovascular events in patients by 25%. *See* Todd Campbell, *Is It Time to Ditch Your Fish Oil Pills for this "Miracle" Medicine?*, Motley Fool (Sept. 24, 2018). Studies show that this decrease was on top of the 25%-plus reduction historically observed in patients taking statins. *See id.*

Vascepa®'s benefits have also been recognized by government regulators. It is the *only* drug that FDA has approved to reduce cardiovascular risk among patients with elevated triglyceride levels, as an add-on to statin therapy. *See* Press Release, FDA, FDA Approves Use of Drug to Reduce Risk of Cardiovascular Events in Certain Adult Patient Groups (Dec. 13, 2019). It is also the *only* FDA-approved treatment for severe hypertriglyceridemia shown to provide the cardiovascular benefit of lowering bad cholesterol. *See* App. 89a; *see also* Julia Ries, *How the New FDA-Approved Fish Oil Drug Can Help Your Heart*, Healthline.com (Dec. 16, 2019) ("Vascepa significantly lower[s] people's cardiovascular risk and triglyceride levels").

Respected journals and organizations have reported on the significance of Vascepa®'s remarkable testing results. For example, *The New England Journal of Medicine* "welcome[d]" Vascepa®'s testing results "with surprise, speculation, and hope" because

the drug provides such a "substantial benefit with respect to major adverse cardiovascular events." John J.P. Kastelein & Erick S.G. Stroes, *FISHing for the Miracle of Eicosapentaenoic Acid*, 380 N. Engl. J. Med. 89, 89, 90 (2019). In fact, *The New England Journal of Medicine* deemed the study's results to be so significant that its editorial board selected a story on Vascepa®'s clinical results as its top story concerning "the most important research in the field from the past year." Harlan M. Krumholz, NEJM Journal Watch Cardiology *2018 Top Stories* (Dec. 26, 2018). Similarly, the American Heart Association included Vascepa®'s clinical results in its "annual list of major [research] advances in heart disease and stroke." Am. Heart Ass'n, *AHA Names Top Heart Disease and Stroke Research Advances of 2018*, Heart.org (Dec. 31, 2018).

Both the Federal Circuit and the district court brushed aside these important objective indicia that Amarin's invention was not obvious. Their failure to consider the totality of evidence was driven not only by improper 20/20 hindsight, but also more fundamentally by their failure to apply the correct legal standard. The Federal Circuit's burden-shifting approach was dispositive of the outcome of this case.

II. The Question Presented Is Very Important.

The patent system that Congress created seeks to achieve a careful balance between incentivizing pathbreaking inventions and enabling robust competition. In the drug context, this balance is vital to encouraging manufacturers to develop innovative treatments that respond to unmet needs, and to ensuring that innovative treatments are affordable

and accessible to patients. The Hatch-Waxman Act balances these considerations by creating a simplified procedure "to speed the introduction of low-cost generic drugs to market," *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405 (2012), while simultaneously extending patent protection to incentivize companies "to develop and market products." *Pfizer Inc. v. Dr. Reddy's Labs., Ltd.*, 359 F.3d 1361, 1364 (Fed. Cir. 2004). Both components—patent protection and simplified generic approval—are important to the patient community and for improving public health.

Many Americans cannot afford medical services or treatments due to high out-of-pocket costs, causing them to choose between forgoing vital care and taking on significant debt or even bankruptcy. *See* Michael Sainato, *The Americans Dying Because They Can't Afford Medical Care*, Guardian (Jan. 7, 2020). For that reason and others, FDA has taken significant steps to accelerate the approval of generic drugs. The benefits of generic competition, however, cannot be realized unless a novel drug is developed in the first instance and the public knows about it. That is why competitors must wait until patent exclusivity expires before they can sell a generic version of an FDA-approved drug. *See* 35 U.S.C. § 271(e)(3), (4)(A)–(B).

Patent protection is important because it incentivizes pioneering companies to undertake costly research and development to discover new treatments and bring them to market. Bringing a new drug to market requires a massive investment. Indeed, recent estimates suggest that the average research-and-development costs of bringing a new drug to market

are nearly $2.6 billion. *See* Joseph A. DiMasi, Henry G. Grabowski, & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. Health Econ. 20, 31 (2016).

Bringing a new drug to market also entails significant risk, not least because relatively few new drugs are successful. Government studies suggest that only 20 in 5,000 compounds (approximately 0.4%) of screened compounds ever enter preclinical testing in laboratories and on animals. *See* FTC, To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy, ch. 3, at 6 (2003). Moreover, "95% of drugs that enter clinical trials do not make it to the market." Thomas Hartung, *Food for Thought Look Back in Anger – What Clinical Studies Tell Us About Preclinical Work*, 30 ALTEX 275, 275 (2013). In addition, when a compound is found to be adequately safe to test on humans, there are three phases of clinical testing, each of which is required to determine the compound's safety and efficacy. *See* FTC, To Promote Innovation, *supra*, ch. 3, at 6. As a result, developing and commercializing a drug often takes more than a decade. *See* Joseph A. DiMasi & Henry G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 Managerial & Decision Econ. 469, 475 (2007).

Without patent protection, most companies would not undertake the investments necessary to develop an innovative drug for patients, only to face immediate competition from generic versions. Here, for example, Amarin spent "$465 million in research and development" to discover Vascepa®'s second indication to reduce the risk of cardiovascular events

for patients. App. 55a. That second indication represented the culmination of years of clinical development that succeeded where others had failed. *See* Deepak L. Bhatt et al., *Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia*, 380 N. Eng. J. Med. 11, 12 (2019); Press Release, Amarin Corp., Amarin Receives FDA Approval of Vascepa® (Icosapent Ethyl) to Reduce Cardiovascular Risk (Dec. 13, 2019). Even with patent protection, it is reported that Amarin investors do not expect to recoup their investment in Vascepa® until 2024. *See* App. 55a.

Beyond fostering innovation, patent protection also encourages patent holders to educate patients, caregivers, and health-care providers about new treatments. The district court noted that "marketing spending tends to be higher at the beginning of a pharmaceutical product's lifecycle, given the need to educate physicians about the clinical profile of the new drug in question." App. 55a. While that is true, it is also true that when a company conducts additional groundbreaking research, or when a medication receives expanded approval for new indications, renewed efforts are needed to educate patients, caregivers, and health-care providers.

The hard reality is that without patent rights, many patients will remain in the dark. Significantly, although Amarin received initial approval for Vascepa® in 2012, it did not receive its second indication until December 2019 (just months before the district court's judgment). *See* App. 3a, 25a. As a result, health-care providers, caregivers, and patients are only beginning to understand and appreciate the

significance of the new indication. But because Vascepa® is Amarin's only product, the company is unlikely to maintain its nascent educational campaign if its efforts are undercut by generic competition. And generic competitors are unlikely to make up the difference because that is not part of their business model. *See* Curt D. Furberg, Bengt D. Furberg, & Larry D. Sasich, Knowing Your Medications: A Guide to Becoming an Informed Patient 56 (2009) (noting that "generic manufacturers spend much less on marketing and accept much lower profit margins" than brand-name manufacturers").

There is thus an important public need to maintain the incentives for Amarin to educate healthcare providers on the benefits of its pathbreaking drug. Cardiovascular disease has long been the leading cause of mortality in the United States. *See* CDC, *Heart Disease Facts*, CDC.gov (Sept. 8, 2020). Although the number of deaths due to heart disease declined substantially between 2000 and 2010, the trend has since reversed. *See* Sally C. Curtin, *Trends in Cancer and Heart Disease Death Rates Among Adults Aged 45-65: United States 1999-2017*, 68 Nat'l Vital Stat. Rep. 1, 2, Fig. 1 (May 22, 2019); *see also* CDC, *Data Brief No. 254: Changes in the Leading Cause of Death: Recent Patterns in Heart Disease and Cancer Mortality* 1, 1 (Aug. 2016). Nearly 650,000 Americans die from heart disease each year—"that's *1 in every 4 deaths*." CDC, *Heart Disease Facts*, *supra*. About 805,000 Americans suffer a heart attack each year. *Id.* More than 30 million Americans take statins. *See* Peter Wehrwein, *Statin Use Is Up, Cholesterol Levels Are Down: Are Americans' Hearts Benefiting?*, Harv. Health Pub. (Apr. 15, 2011).

Between 50 to 70 million adults in the United States have high levels of triglycerides. Campbell, *Is It Time to Ditch Your Fish Oil Pills*, *supra*. These statistics coincide with the CDC last year listing "heart conditions" as presenting an "increased risk of severe illness from the virus that causes COVID-19." CDC, *COVID-19, People with Certain Medical Conditions*, CDC.gov (Dec. 29, 2020).

Information presented by Amarin's scientists to the American College of Cardiology suggests that Vascepa® may help prevent more than 70,000 cardiovascular events each year in adults in the United States with known cardiovascular disease or diabetes. *See* Press Release, Amarin Corp., Amarin Highlights VASCEPA® (Icosapent Ethyl)-Related Data Presented at American College of Cardiology's Annual Scientific Session Together with World Congress of Cardiology (ACC.20/WCC) (Mar. 31, 2020). Moreover, because Vascepa® is "highly cost-effective," it could be the "rare[]" therapy that results in "net healthcare cost-savings to patients, payers and society." *Id.*

There is thus "no doubt that" Amarin's Vascepa® "is a medication that could benefit a substantial portion of the U.S. and meets an unmet need." Trisha Roy & Saumya Joseph, *FDA Panel Unanimously Backs Expanding Use of Amarin's Heart Drug Vascepa®*, Reuters (Nov. 14, 2019) (quoting Dr. Jack Yanovski of the National Institutes of Health). It represents a significant step forward—an innovative advance in the treatment of cardiovascular disease and severe hypertriglyceridemia—that is now available to meet a previously unmet need for

patients, provided that Amarin continues to invest in publicizing its life-saving drug so that patients, caregivers, and health-care practitioners are adequately aware of the medication's benefits. In short, Vascepa® is precisely the type of invention that patent law is designed to encourage and protect. The Federal Circuit's decision to the contrary is worthy of this Court's review.

* * *

The Federal Circuit has made up a test for which there is no support and on which actual public-health outcomes turn. If the Federal Circuit's precedential departures are not corrected, they will undermine the patent system by discouraging pioneering companies from pursuing the development of innovative treatments for serious diseases. As a result, new medications that treat otherwise unmet medical needs may not be available to the patients who need them. More immediately, without patent protections, Amarin will be unable to continue making the investments needed to educate patients, caregivers, and health-care providers about Vascepa®'s clinical trial results and its newly discovered benefits. In addition, many health-care practitioners may never become aware of, and therefore may not prescribe, a treatment to patients for whom Vascepa® may be medically necessary.

CONCLUSION

This Court should grant the petition for certiorari.

Respectfully submitted,

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