No. 20-1723

IN THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

AMARIN PHARMA, INC.,
AMARIN PHARMACEUTICALS IRELAND LTD.,

Plaintiffs/Appellants,

v.

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

Defendants/Appellees.

Appeal from the United States District Court for the District of Nevada,
No. 2:16-CV-02525-MMD, Hon. Miranda M. Du

BRIEF OF AIMED ALLIANCE AS *AMICUS CURIAE* IN SUPPORT OF APPELLANTS

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May 19, 2020

CERTIFICATE OF INTEREST

Counsel for *amicus curiae* certifies the following:

1. The full name of every *amicus* represented by me:

   Aimed Alliance

2. The name of the real party in interest represented by me:

   Aimed Alliance

3. Parent corporations and publicly held companies that own 10% or more of stock in the party:

   N/A. Aimed Alliance is a 26 U.S.C. § 501(c)(3) not-for-profit organization.

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

   Ashley C. Parrish, Paul Alessio Mezzina, and Jesse D.H. Snyder of King & Spalding LLP

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will affect or be directly affected by this court's decision in the pending appeal. *See* Fed. Cir. R. 47.4(a)(5) and 47.5(b). (The parties should attach continuation pages as necessary):

   None

Respectfully submitted,

/s/ *Ashley C. Parrish*
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May 19, 2020

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STATEMENT OF INTEREST

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 often 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 plaintiffs-appellees Amarin Pharma, Inc. and Amarin Pharmaceuticals Ireland Limited, is one of those stakeholders.

Aimed Alliance is familiar with Amarin's Vascepa® product and the 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 the 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 in this case that is not offered by any party. Aimed Alliance submits this brief in hopes that it will aid the Court in assessing the potential ramifications of the district court's decision beyond its impact on the parties directly involved.

STATEMENT OF COMPLIANCE WITH RULE 29(A)

This brief is submitted in accordance with Rule 29(a) of the Federal Rules of Appellate Procedure. All parties have consented to the filing of the brief. *See* Fed. Cir. R. 29(c).

No party or party's counsel authored this brief in whole or in part; no party or party's counsel contributed money to fund the preparation or submission of this brief; and no other person except *amicus curiae*, its members, or its counsel contributed money intended to fund the preparation or submission of this brief. *See* Fed. R. App. P. 29(a)(E).

INTRODUCTION AND SUMMARY OF ARGUMENT

Ensuring that patients are able to access safe and effective medicines is one of the cornerstones of federal drug patent law. By invalidating Amarin's patents, the district court's order threatens that access. If it is not corrected, the decision will undermine the incentives that Congress created for companies to invest in developing innovative medications for patients in need. It may also reduce the number of patients who are informed about, and subsequently are treated with, Amarin's innovative therapy, placing those patients at a higher risk for heart attack, stroke, and cardiovascular death.

The district court invalidated Amarin's patents for Vascepa®, the first FDA-approved drug to treat severe hypertriglyceridemia without increasing bad cholesterol levels and "the first FDA approved drug to reduce cardiovascular risk among patients with elevated triglycerides levels as an add-on to maximally tolerated statin therapy." Press Release, FDA, *FDA Approves Use of Drug to Reduce Risk of Cardiovascular Events in Certain Adult Patient Groups* (Dec. 13, 2019). The district court based its invalidation decision on its conclusion that Amarin's patents were obvious. That conclusion cannot be reconciled,

however, with research showing that Vascepa® is a one-of-a-kind innovation that improves treatment options available to patients with severe hypertriglyceridemia and to patients with elevated triglyceride levels who also take statins — both life-threatening medical conditions. The district court's decision is contrary to Congress's statutory objectives, misapplies this Court's precedents, and is not in the interest of patients.

1. Congress has created a patent system for drugs that balances the goals of, on one hand, fostering medical and pharmaceutical innovation and, on the other, ensuring that patients have ready access to the medications they need. The statutory scheme achieves that delicate balance by providing companies with patent rights for the novel drugs they develop, while simplifying the generic drug approval process for medications not subject to patent protections. Favoring one side of the balance over the other threatens the system that Congress designed to protect public health.

Protecting patent rights is important to patients for two reasons. First, it incentivizes companies to invest massive sums — on average more than $2 billion — in research and development to discover and bring innovative medications to market that can meet patients' unmet

medical needs. Second, it encourages manufacturers, after a new medication is approved by FDA, to undertake the investments necessary to inform and educate patients, caregivers, and health care providers to ensure that their new medication is able to reach the patients for whom it is medically necessary. These goals depend on a period of patent exclusivity. Equally as important, generic manufacturers may offer lower cost, therapeutic equivalent medications, improving access further for patients, but they are only permitted to do this after the period of patent exclusively ends.

2. As explained in more detail below, Vascepa® has been widely recognized as a significant advance in the treatment of cardiovascular disease. Before Vascepa®, individuals who suffered from severe hypertriglyceridemia — a genetically based, life-threatening disease — could treat their disease only by taking medications that raised bad cholesterol. Although health care practitioners, scientists, and other experts had studied and known about this problem for decades, no one could find a solution — until Amarin conceived of, and made the investments necessary to develop, Vascepa®.

After receiving FDA approval, Amarin continued to invest in Vascepa® by conducting a massive, long-term trial that resulted in another discovery: Vascepa® reduces the risk of major cardiovascular events in statin-treated patients with elevated triglyceride levels *by 25%*. The trial showed "for the first time that triglyceride reduction with an appropriate therapy . . . when used in appropriate doses can make a significant difference." Catherine Hackett, *"Phenomenal" REDUCE-IT Establishes Triglyceride Theory,* MDedge.com (Nov. 20, 2018). Given the number of people who have persistent elevated triglyceride levels, and the ability of Vascepa® to lower the risk of cardiovascular events, researchers have noted that Vascepa® "has huge implications" for patients. Anahad O'Connor, *Fish Oil Drug May Prevent Heart Attack and Strokes in High-Risk Patients*, N.Y. Times (Sept. 25, 2018).

3. The district court's decision invalidating Amarin's patents warrants reversal. The district court gave too little weight to the presumption of patent validity, improperly shifted both the burden of production and persuasion to Amarin, and discounted objective indicia that the asserted claims were nonobvious. Most notably, the court gave insufficient weight to the undisputed facts that the problem of treating

severe hypertriglyceridemia without increasing bad cholesterol had been recognized for decades, and that no drug was available to solve this problem until Amarin developed Vascepa®. In short, the district court "slipp[ed] into the use of hindsight" in concluding that Amarin's innovative drug is obvious. *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1052 (Fed. Cir. 2016) (en banc) (quoting *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 36 (1966)). That decision is wrong and should be reversed.

ARGUMENT

I. Patents Benefit Patients by Incentivizing Drug Companies to Develop New Drugs and Educate the Public about New Treatments.

The patent system 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 those innovative treatments are affordable and accessible to patients. The Hatch-Waxman Act balances these considerations in two ways. First, the Act creates a "simplified procedure for FDA approval of generic drugs." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998). Second, the Act extends 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, the FDA has taken significant and necessary steps to accelerate the approval of generic drugs. Nevertheless, the benefits of generic competition 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 is nearly $2.6 billion. 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, as relatively few new drugs are successful. Government studies suggest, for example, that only 20 in 5,000 compounds (approximately 0.4%) of screened compounds ever enter preclinical testing in laboratories and on animals. FTC, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, ch. 3, at 6 (Oct. 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 that are required to determine the compound's safety and efficacy. FTC, *To Promote Innovation*, *supra* p. 10. 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); *see also* Cynthia M. Ho, Access to Medicine in the Global Economy: International Agreements on Patents and Related Rights 7 (2011).

Without patent protection, most companies would not undertake the effort and 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. Appx41. That second indication, funded by hundreds of millions of dollars of high-risk investments, represented the culmination of years of clinical development that succeeded where others had not succeeded. *See generally* 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* Appx40.

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." Appx41. While that is undoubtedly 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.

Despite Vascepa® receiving initial FDA approval in 2012, Amarin did not receive its new indication for Vascepa® until December 2019. *See FDA Approves Use of Drug*, *supra* p. 4. As a result, the American Diabetes Association only recently updated its "Standards of Medical Care for Diabetes" to incorporate the findings of the REDUCE-IT study and to make new recommendations regarding the prescribing of Vascepa®. *See* Press Release, Am. Diabetes Ass'n, *American Diabetes Association® Issues Critical Updates to the 2019 Standards of Medical Care in Diabetes* (Mar. 27, 2019). Similarly, it was only in September

2019 that the National Lipid Association issued a position statement recognizing the cardiovascular risk-lowering effects of Vascepa® based on the REDUCE-IT study. *See* Carl E. Orringer, Terry A. Jacobson, Kevin C. Maki, *National Lipid Association Scientific Statement on the Use of Icosapent Ethyl in Statin-Treated Patients with Elevated Triglycerides and High or Very-High ASCVD Risk*, 13 J. Clinical Lipidology 860, 861 (2019). These recent developments underscore that patients, caregivers, and health care providers are only beginning to understand and appreciate the significance of the new indication approved by FDA for Vascepa®. As a result, additional educational efforts are needed, even though the medication has been on the market for several years.

Congress specifically recognized this concern with Vascepa®. After discussing that "[c]ardiovascular events account for one of every three deaths in the United States," a House Report noted that "[a] clinical trial called REDUCE-IT has demonstrated a 25 percent relative risk reduction in major cardiovascular events." H.R. Rep. No. 116-62, at 87 (2019). Yet, "despite these statistics, many individuals do not regularly access [this type of] treatment[]." *Id.*

The hard reality is that without patent rights, many patients will remain in the dark. Given that Vascepa® is Amarin's only product, the company is unlikely to maintain its nascent, months-old educational campaign for patients, caregivers, and health care providers if its efforts are undercut by generic competitors. Moreover, generic competitors are unlikely to make the investments necessary to educate patients, caregivers, and health care providers because that is not part of their business model. *See* Curt D. Furberg, Bengt Furberg, & Larry 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").

II. Vascepa® Has Had a Transformative Effect on Treating Severe Hypertriglyceridemia and Heart Disease.

Vascepa® has been recognized as a "groundbreaking" drug. *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). It has been given that recognition because, unlike other medications, it has been shown to (1) treat severe hypertriglyceridemia

without increasing bad cholesterol and (2) reduce the risk of major cardiovascular events in statin-treated patients with persistent elevated levels of triglycerides.

In 2012, the FDA first approved Vascepa® to treat severe hypertriglyceridemia. *See* FDA, Ctr. for Drug Eval. & Research, New Drug Application Approval Package for: VASCEPA™ 1, 1 (July 26, 2012). Patients who suffer from severe hypertriglyceridemia are at heightened risk of acute pancreatitis, a potentially life-threatening condition. *See* Harsha Karanchi & Kathleen Wyne, Hyper-triglyceridemia (Feb. 17, 2019). High levels of triglycerides can also play a role in the hardening of arteries or thickening of the artery wall, which can increase the risk of a heart attack or stroke. *See FDA Approves Use of Drug*, *supra* p. 4.

Before Vascepa®, other available treatments for severe hypertriglyceridemia increased bad cholesterol, a major cause of cardiovascular disease. *See* Appx5 (explaining that treatment other than Vascepa "dramatically increase[d] LDL-C levels"). Vascepa®'s novel solution was to mitigate this harmful tradeoff. *See* Adam Feuerstein, *Amarin Prescription Fish-Oil Pill Approved*, The Street (July 26, 2012).

Where many others had tried and failed, Amarin's invention demonstrated success. *See* O'Connor, *supra* p. 7 ("Many cardiovascular experts were doubtful that adding fish oil on top of statins would produce much if any benefit because a number of smaller and less rigorous studies over the year had failed."). In doing so, it met a "long-felt need for a drug . . . that could reduce [triglyceride] levels without raising [bad cholesterol] levels." Appx67.

Vascepa® also provides patients with additional innovative benefits. After conducting a clinical trial following more than 8,000 patients for approximately five years, researchers discovered that Vascepa® reduces cardiovascular risk in statin-treated patients with persistent elevated triglycerides. Cardiovascular disease is the leading killer of both men and women in the United States. *See* CDC, *Heart Disease Facts* (Dec. 2, 2019). 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 a major cardiovascular event 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.*

In December 2019, after giving Amarin's supplemental application "priority review," the FDA-approved Vascepa® for an additional indication — "as an adjunctive (secondary) therapy to reduce the risk of cardiovascular events among adults with elevated triglyceride levels (a type of fat in the blood) of 150 milligrams per deciliter or higher." *FDA Approves Use of Drug*, *supra* p. 4; *see also* FDA, *Priority Review* (Jan. 4, 2018) (explaining that the FDA grants priority review only "if approved, would [the drug] be [a] significant[] improvement[] in the safety or effectiveness of the treatment . . . when compared to standard applications"). Vascepa® is the first and only drug that the FDA has approved to reduce cardiovascular risk among patients with elevated triglyceride levels, as an add-on to statin therapy. *See FDA Approves Use of Drug*, *supra* p. 4. It is also the only FDA-approved treatment for severe hypertriglyceridemia shown to provide the cardiovascular benefit of lowering bad cholesterol. *See* Appx67 (describing how Vascepa filled an unmet need); *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 its 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).

The need for Amarin's innovative drug is also significant. Cardiovascular disease has long been the leading cause of mortality in the United States. *See* CDC, *Heart Disease Facts*, *supra* p. 16. 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 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* p. 16. 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, *supra* p. 16.

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, therefore, "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.

III. The District Court's Obviousness Analysis Is Flawed.

The approach taken by the district court — invalidating Amarin's patents on the grounds that Vascepa® innovations were obvious — undermines incentives for innovation that the patent system seeks to reinforce. There are many inventions that might seem obvious with twenty-twenty hindsight, but that has never been the proper approach to evaluating patents.

The point of the obviousness inquiry is to identify advancements that are so slight or trivial that they would have occurred in any event without the need for patent protection. *See, e.g., 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 skilful [sic] mechanic, not that of the inventor"). "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.'" *Dow Jones & Co.*

v. Ablaise Ltd., 606 F.3d 1338, 1349 (Fed. Cir. 2010) (quoting 35 U.S.C. § 103(a)). The analysis requires a court to take account of all relevant factors, including objective indicia of non-obviousness, before any conclusion is reached. *See Apple*, 839 F.3d at 1050.

The district court lost sight of what the obviousness inquiry is intended to accomplish. *See Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1292 (Fed. Cir. 2012) (affirming validity and noting the flexible nature of the obviousness inquiry"). A drug that indisputably addresses a previously unmet medical need, took hundreds of millions of dollars to develop, and was heralded as a "game changer" for patients is not a trivial invention too obvious to be entitled to patent protection. Hackett, *supra* p. 7 (describing Vascepa® as a "game changer").

The district court failed to reach this conclusion because it failed to apply the proper burden. "[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). 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 by the challenger, *id.* at 103, the Supreme Court made plain the longstanding requirement 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 district court adopted an improper burden-shifting framework. It first concluded that a prima facie case of obviousness existed and then shifted both the burden of production and persuasion to Amarin to show that secondary considerations militate against that prima facie showing: "Defendants met their clear and convincing burden to prove their *prima facie* obviousness case at trial, the Court turns to consideration of Plaintiffs' proffered secondary considerations." Appx61.

That is not the standard for obviousness. Under this Court's precedents, if a challenger succeeds in establishing a prima facie case of obviousness, the patent holder is entitled to come forward with objective indicia of non-obviousness and then, after all of the evidence is in the

record, the challenger must prove by clear and convincing evidence that the patent is obvious. *See ZUP LLC v. Nash Mfg., Inc.*, 896 F.3d 1365, 1373 (Fed. Cir. 2018).

Here, in contrast, the district court legally erred by requiring Amarin to both produce and persuade. In particular, the decision required Amarin to reestablish — with even more evidence and greater persuasion — the validity of an already issued patent. That result undermines Congress's incentives to promote innovation for the benefit of consumers.

It also shows why this Court has time and again rejected burden-shifting when deciding obviousness. As this Court has emphasized, "the Supreme Court has never imposed nor even contemplated a formal burden-shifting framework in the patent litigation context." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1075 (Fed. Cir. 2012) (reversing district court's determination of obviousness because "the court imposed a burden-shifting framework in a context in which none exists"). To be sure, this Court has suggested that "a burden-shifting framework makes sense in the prosecution context," *id.* at 1080 n.7, and that the patentee "bears the

burden of production with respect to evidence of secondary considerations." *ZUP*, 896 F.3d at 1373. But "precedent is clear that 'the burden of persuasion remains with the challenger during litigation because every issued patent is entitled to a presumption of validity.'" *Id.* (quoting *Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd.*, 719 F.3d 1346, 1353 (Fed. Cir. 2013)). The reason that the burden of persuasion always rests with the patent challenger is to avoid perverse outcomes, such as this one, where a first-of-its-kind drug is deemed with hindsight to be something that anyone of ordinary skill could have achieved.

* * *

If the district court's decision is left uncorrected, it will discourage pioneering companies from pursuing the development of innovative treatments for serious diseases because they will be unable to rely on their patents to recover their costs. 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 the treatment to patients for whom Vascepa® may be medically necessary. This Court can and should defuse these risks by reversing the decision below.

CONCLUSION

The Court should reverse the district court's judgment.

Respectfully submitted,

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May 19, 2020

CERTIFICATE OF COMPLIANCE

I hereby certify that this brief complies with the type-volume limitation of Fed. R. App. P. 32(g)(1), Fed. R. App. P. 32(a)(7)(B), and Fed. R. App. 29(a)(5) because this brief contains 4,677 words, excluding the parts of the brief exempted by Fed. R. App. P. 32(f).

This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionately spaced typeface using Microsoft Word Century Schoolbook 14-point font.

Respectfully submitted,

/s/ *Ashley C. Parrish*
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Counsel for Amicus Curiae Aimed Alliance

Dated: May 19, 2020

CERTIFICATE OF SERVICE

In accordance with Fed. R. App. P. 25 and Fed. Cir. R. 25, I hereby certify that on May 19, 2020, I caused the foregoing to be filed with the Court electronically using the CM/ECF system, which will send a notification to all counsel of record.

Respectfully submitted,

/s/ *Ashley C. Parrish*
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Dated: May 19, 2020