No. 20-1119

In the Supreme Court of the United States

AMARIN PHARMA, INC. ET AL., PETITIONERS

v.

HIKMA PHARMACEUTICALS USA INC., ET AL.

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

BRIEF IN OPPOSITION

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QUESTION PRESENTED

This case involves six substantively identical patents related to EPA—an omega-3 fatty acid that is found naturally, along with DHA, in fish oil. None of the patents claim EPA itself or its use to reduce triglycerides. As Amarin admits, "EPA had long been used to treat lipid disorders, and so there were clinical studies showing the beneficial effects of EPA in treating hypertriglyceridemia" in the prior art. Pet. 10–11 n.2. Instead, the patents claim a method of treating a patient with severe hypertriglyceridemia (i.e., triglycerides ≥500 mg/dL) by administering 4 g/day of EPA for at least 12 weeks. App. 46a.

After a seven-day bench trial, the district court found Amarin's patents obvious. Quoting this Court's decision in *Graham* v. *John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966), the district court examined "four underlying factual determinations: (1) 'the scope and content of the prior art'; (2) 'the level of ordinary skill in the pertinent art'; (3) the 'differences between the prior art and the claims at issue'; and (4) '[s]uch secondary considerations as commercial success [and] long-felt but unsolved needs.'" App. 73a. After weighing all the evidence, the district court held that "in view of all four *Graham* factors (including alleged secondary considerations), Defendants have proven by clear and convincing evidence that all Asserted Claims are invalid as obvious under 35 U.S.C. § 103." App. 92a. The Federal Circuit summarily affirmed in a one-line, nonprecedential order. App. 1a–2a.

Against this backdrop, the question presented is whether the courts below erred in weighing the evidence to find that the particular method of treatment claimed in Amarin's patents was obvious.

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Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals International Limited are indirect wholly owned subsidiaries of Hikma Pharmaceuticals PLC. Hikma Pharmaceuticals PLC is publicly listed. No other publicly held companies own 10% or more of the stock of Hikma Pharmaceuticals USA Inc. or Hikma Pharmaceuticals International Limited.

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INTRODUCTION

Amarin's petition rests on the premise that the Federal Circuit here "depart[ed]" from this Court's precedent by adopting an obviousness framework that "relegates objective indicia to second-class status" and "erroneously shifts the burden of proof to the patentee to show nonobviousness." Pet. 3–4. That premise is false. The Federal Circuit's decision is a one-line, nonprecedential order that does not raise any issue at all, let alone the petition's question presented. And the district court's decision that it affirmed is a fact-intensive ruling that applies settled obviousness precedent, breaks no new ground, and raises no question of any importance beyond Amarin's patents. The Court should deny certiorari.

Citing *Graham* v. *John Deere Co. of Kansas City*, 383 U.S. 1 (1966)—Amarin's lead case—the district court expressly recognized that its "obviousness inquiry must * * * consider whether objective indicia of non-obviousness support the Asserted Claims." App. 47a. Based on an expansive record spanning a seven-day trial, the district court carefully evaluated Amarin's alleged evidence of secondary considerations (App. 47a–59a, 81a–92a) but concluded as a factual matter that, "at best," Amarin's evidence was "weak" (App. 92a). After weighing all the evidence, the district court reached its conclusion of obviousness: "For the reasons discussed above, in view of all four *Graham* factors (including alleged secondary considerations), Defendants have proven by clear and convincing evidence that all Asserted Claims are invalid as obvious under 35 U.S.C. § 103." *Ibid.*

Amarin's petition never cites the district court's conclusion. It urges this Court to grant certiorari to

"instruct[] courts to analyze the totality of the evidence, including all four *Graham* factors together, before concluding that an invention is obvious" (Pet. 16), yet ignores that this is precisely what the district court did. Even if the district court had misapplied the *Graham* framework (which it did not), certiorari is not warranted to correct "the misapplication of a properly stated rule of law." Rule 10. Simply put, Amarin's "question presented" is not presented at all—by either decision below.

This case is also a poor vehicle for reviewing the question presented because no matter how that question is answered, it would not change the outcome. This Court has long held that secondary "considerations are relevant only in a close case where all other proof leaves the question of invention in doubt"—not where "the lack of invention is beyond doubt and cannot be outweighed by such factors." *Dow Chem. Co*. v. *Halliburton Oil Well Cementing Co*., 324 U.S. 320, 330 (1945). This case was far from "close." The district court made extensive factual findings that the evidence of obviousness was "clear and convincing," "persuasive," and supported by "key premises that [Amarin's own expert] conceded." App. 76a–77a. Amarin's counterarguments were "unavailing" and "lack[ed] evidentiary support." App. 79a–80a. Amarin does not challenge any of these factual findings, which would render Amarin's patents invalid under *Graham* regardless of how any alleged secondary considerations are weighed.

Even if the question presented were both implicated by the decisions below and material to the outcome, certiorari would still be unwarranted because the "prima facie framework" that Amarin purports to challenge is consistent with this Court's precedent.

Amarin contends it is improper to reach an initial finding of obviousness and then "look to the patentee's proof of objective indicia to see if it rebuts the conclusion the court has already reached." Pet. 3. Yet that is how this Court has always treated such "secondary factors," including in *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398, 426 (2007). There, the Court first determined that "[t]he prior art * * * leads us to the conclusion that [the claimed invention] would have been obvious." *Id.* at 425. After making that finding, the Court concluded that the patentee "has shown no secondary factors to dislodge the determination that [the claimed invention] is obvious." *Id.* at 426. Amarin's proposed bar against any "initial conclusion of obviousness" based on the prior art (Pet. 21) cannot be reconciled with *KSR*.

Nor is there any conflict within the Federal Circuit. Amarin relies extensively on a dissent by Judge Reyna in *Intercontinental Great Brands LLC* v. *Kellogg North America Co.*, 869 F.3d 1336 (Fed. Cir. 2017) (Pet. 2–3, 22–23), but ignores that Judge Reyna was on the panel below and voted to affirm. App. 1a. Not a single Federal Circuit judge voted to rehear this case—or even called for a response to Amarin's rehearing petition. App. 95a–96a. And while Amarin tries to fabricate a conflict with the Federal Circuit's decision in *In re Cyclobenzaprine* (Pet. 22), that decision recognized that "even panels that have used the 'prima facie' * * * language generally have made clear that a fact finder must consider *all* evidence of obviousness and nonobviousness before reaching a determination." *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Pat. Litig.*, 676 F.3d 1063, 1077 (Fed. Cir. 2012). In short, any purported distinction between the "prima facie" and "totality"

frameworks (Pet. 4–5) is purely semantic—there is no substantive conflict for this Court to resolve.

Certiorari should be denied.

STATEMENT

To understand the role of secondary considerations of nonobviousness (also called "objective indicia" of nonobviousness), it is helpful to review this Court's well-settled approach to analyzing obviousness. In *Graham*, this Court held that obviousness turns on "several basic factual inquiries," including "the scope and content of the prior art," "differences between the prior art and the claims," and "the level of ordinary skill in the pertinent art." 383 U.S. at 17. "Against this background, the obviousness or nonobviousness of the subject matter is determined." *Ibid.*

While purporting to apply *Graham*, Amarin never addresses any of these core "factual inquiries." Nor does it challenge any of the district court's extensive findings on the prior art's teachings. Instead, Amarin focuses solely on secondary considerations. In *Graham*, this Court explained that "[s]uch secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter" and, in some cases, "may have relevancy." 383 U.S. at 17–18. In cases where the claimed invention is "clearly evident from the prior art," however, secondary considerations "do not * * * tip the scales of patentability." *Id.* at 36. As shown below, that is the case here.

Amarin's asserted patents all claim the same method of treatment—administering 4 g/day of pure EPA to a patient with severe hypertriglyceridemia (i.e., triglycerides ≥500 mg/dL) for at least 12 weeks.

App. 46a. Nothing about this treatment method was new or even invented by Amarin, and the factual record overwhelmingly proves that it was obvious.

A. Lovaza, an EPA-DHA mixture, was approved for severe hypertriglyceridemia, but had a side effect of raising LDL-C.

This case is about fish oil. Beginning in the 1970s, fish-based diets were "linked to low incidence of coronary heart disease." C.A.J.A. 88501, 88505 nn.1–8. Through the 1980s, studies on "fish oils rich in [omega]-3 fatty acids were conducted and a reduction of plasma triglyceride levels was demonstrated." C.A.J.A. 88365, 88371 n.6. Scientists found that EPA and DHA—omega-3 fatty acids that occur naturally in fish oil—"consistently reduce serum triglyceride levels." C.A.J.A. 88504. Fish oil has thus long been used to treat patients with hypertriglyceridemia.

Medical guidelines "define 'normal triglycerides' as less than 150 mg/dL, with levels above that considered elevated to various degrees." App. 6a. "Severe hypertriglyceridemia" refers to patients with "levels above 500 [mg/dL], regardless of why." App. 7a. Doctors use triglyceride-lowering agents in patients with severe hypertriglyceridemia because it carries "an elevated risk of acute pancreatitis"—"an excruciatingly painful and potentially life-threatening condition." *Ibid.* At trial, "all experts agreed that the [500 mg/dL] threshold simply represents a marker for the risk of pancreatitis, which has nothing to do with LDL-C levels"—i.e., "the 'bad' cholesterol that physicians try to reduce in their patients with drugs such as statins." App. 81a, 6a.

In 1997, a pharmaceutical-grade fish-oil product, initially called "Omacor" but later renamed "Lovaza,"

was developed in the United States. C.A.J.A. 88356, 1344–1345. By March 2008 (the alleged priority date for Amarin's patents), "Lovaza was 'widely used' and 'a very successful drug.'" App. 33a. In 2007, the FDA-approved label for Lovaza was published in the "Physicians' Desk Reference" ("PDR"), a well-known compilation of drug labels. C.A.J.A. 88408–88411. The PDR disclosed that Lovaza contained both EPA and DHA. App. 32a. It further taught that Lovaza was clinically administered for 16 weeks, that its FDA-approved dose was 4 g/day, and that it was "indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with very high (≥500 mg/dL) triglyceride levels"—i.e., severe hypertriglyceridemia. C.A.J.A. 88409–88410; App. 32a–34a.

The PDR warned that Lovaza "may result in elevations in LDL-C * * * in some individuals." App. 34a. The district court found, and Amarin admits, that "[d]octors frequently prescribed statins to treat the increase in bad cholesterol" associated with Lovaza. Pet. 9; App. 34a. Amarin's expert "agreed," however, that "since those patients would have to take two pills, the Lovaza and a statin, a skilled artisan would have been motivated to develop a single pill that treats severe hypertriglyceridemia without LDL-C increases." App. 76a–77a (quotations omitted).

B. Clinical studies in the prior art taught that EPA, unlike DHA, reduces triglycerides without increasing LDL-C.

A "single pill" consisting of pure EPA—without the DHA found in Lovaza and in natural fish oil—was first sold in Japan in the 1990s by Mochida Pharmaceuticals under the brand name "Epadel." C.A.J.A. 88326. By 2000, "EPADEL capsules con-

tain[ed] over 96.5%" pure EPA. C.A.J.A. 88401. By January 2008, "99.9% [pure] EPA" was available. App. 78a. In Japan, Epadel was approved to treat "an excess of triglycerides," which includes severe hypertriglyceridemia. C.A.J.A. 88327, 1346–1347.

Numerous clinical studies in the prior art consistently found that pure EPA reduces triglycerides *without* increasing LDL-C. *E.g.*, C.A.J.A. 1319–1334, 88589–88598, 88501–88504, 88367–88369, 88349, 88480–88485, 88402–88403. In contrast, the prior art taught that "[m]ost previous studies of DHA supplementation have shown increases in LDL cholesterol." C.A.J.A. 88420, 1343–1344. Prior-art studies thus expressly "suggested that EPA and DHA have different properties against lipoprotein metabolism," including on LDL-C. C.A.J.A. 88501, 1323.

The differences between EPA and DHA were explored by Mori, who compared 4 g/day EPA to 4 g/day DHA. C.A.J.A. 88480–88483. As the district court found, "Mori taught that DHA increased LDL-C, whereas 4 g/day of 96% purified EPA reduced triglycerides without increasing LDL-C." App. 47a. "Other prior art * * * similarly taught that EPA did not increase LDL-C in patients with triglyceride levels up to 400 mg/dL." *Ibid.* Expert testimony at trial confirmed that these prior-art studies provided "very strong evidence that DHA, one of the two components of Lovaza * * * , is very likely responsible for the increase in LDL," while "strongly suggest[ing] that EPA is [LDL-]neutral." C.A.J.A. 1344.

Contrary to Amarin's arguments (Pet. 2), EPA was not unique in reducing triglycerides in severely hypertriglyceridemic patients without raising LDL-C. Statins were known to have the same effect. C.A.J.A.

102640–102641, 2609–2611, 1452, 1471–1472, 1509. While Amarin cites examples of LDL-C increases from fibrates and Lovaza (Pet. 9), the cited data involved patients with triglycerides above 700–800 mg/dL, which is considerably higher than the 500 mg/dL threshold in Amarin's patent claims. C.A.J.A. 108954–108955, 43940, 48910, 2611, 2613–2615. Regardless, both sides' experts agreed that data on fibrates, niacin, and Lovaza cannot be extrapolated to pure EPA, which is chemically unrelated to fibrates or niacin and does not contain DHA. C.A.J.A. 2598, 2595, 1400–1401, 1509–1511, 88670.

Given the many studies on EPA and Epadel's commercial availability, dosing for EPA was well established by March 2008. A 2007 patent application by Mochida taught that EPA doses were "typically 0.3 to 6 g/day," with one "preferabl[e]" dose being "3.6 g/day"—i.e., about 4 g/day. C.A.J.A. 88213, 1349–1350. At trial, Amarin's expert admitted that "at least six prior art references * * * disclosed the use of 4 grams per day of purified EPA." C.A.J.A. 2649.

Amarin admits that "EPA had long been used to treat lipid disorders, and so there were clinical studies showing the beneficial effects of EPA in treating hypertriglyceridemia," but falsely states that "none of those studies involved patients with *severe* hypertriglyceridemia." Pet. 10–11 n.2. In fact, at least five prior-art studies on pure EPA included patients with triglycerides above 500 mg/dL. C.A.J.A. 88367 (300 ± 233 mg/dL), 88609 (650, 700, 1225 mg/dL), 88445 (1510 mg/dL), 88543–88544 (513 mg/dL), 88491 (6.31 mmol/L (≈560 mg/dL), 2656–2657, 1351–1352.

C. Amarin relied exclusively on prior-art studies to develop its Vascepa product.

Beginning in 2007, an Amarin employee named Mehar Manku made "contact with a scientist [at] Mochida [the maker of Epadel] to ask for their view of differences between pure EPA and EPA/DHA." C.A.J.A. 91241. Manku received "detailed information from Mochida on EPA's effects on LDL[-C]" and, in his words, was told "Mochida haven't seen any increase in LDL[-C]." C.A.J.A. 90228, 90231.

In emails dated March 2008, Manku summarized what Mochida told him: "we know from Japanese preclinical and clinical studies [that] EPA does not increase LDL as [does] Omacor [i.e., Lovaza]." C.A.J.A. 90691. Citing prior-art studies, Manku observed that "LDL cholesterol has not been reported to rise after pure EPA," and "publications from M[o]chida on EPADEL" showed that "LDL-[C] is reduced." C.A.J.A. 90238, 90566. These emails summarizing the prior art are the only evidence that Amarin cited during discovery to support its allegation that Manku invented the patented treatment on March 25, 2008. C.A.J.A. 109201, 91491 n.13.[1]

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[1] Amarin now tells a different story—that Manku relied on "non-public clinical trials where EPA was used to treat neuropsychiatric conditions such as depression and schizophrenia." Pet. 10. This conception story is not only waived, but meritless. Amarin told FDA that its central nervous system ("CNS") studies found "[n]o consistent changes in triglyceride and cholesterol levels," "were not designed to recruit and evaluate patients with high triglyceride levels," and did not measure blood levels "in a fasting state," among other "major limitations." C.A.J.A. 90362. At trial, expert testimony confirmed that there is

Even before this alleged conception date, an Amarin memo dated March 10, 2008, recognized that "[i]n view of the extensive clinical experience with ultra[-] pure EPA * * * only further limited clinical data are required to confirm the efficacy and safety of ethyl-EPA as a treatment of severe hypertriglyceridemia." C.A.J.A. 90295. Another memo, dated March 20, 2008, acknowledged that Epadel was "identical" to Vascepa (then called "AMR101") and that the "one differentiating feature" between Epadel and Lovaza "is their respective effect on LDL." C.A.J.A. 90421, 95532. Amarin recognized that while "Lovaza treatment may result in elevations in LDL in some individuals," "Epadel treatment does not appear to have the same [e]ffect on LDL levels. * * * Hence[,] there is no reference to Epadel treatment causing LDL elevation in Epadel's packaging insert." C.A.J.A. 90421–90422. Amarin noted that this was confirmed by "Mochida's studies on Epadel, as well as independent studies." C.A.J.A. 90422. As Amarin acknowledged, Mori taught that while "both EPA and DHA reduced triglycerides," only "DHA was also associated with an increase in LDL cholesterol." C.A.J.A. 90428.

In June 2008, less than three months after Amarin's alleged conception date and more than two years before it had any clinical data of its own on hypertriglyceridemia, Amarin told FDA that a "large body of evidence supports the efficacy of Ethyl-EPA, administered either as monotherapy or add-on to statin therapy, in reducing triglyceride levels in patients with dyslipidemia of varying severity." C.A.J.A. 90362. Amarin represented that "[i]n clinical studies per-

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"no connection whatsoever" between "the CNS effects of EPA" and severe hypertriglyceridemia. C.A.J.A. 1512.

formed with Ethyl-EPA to date * * * there is no evidence of a significant rise in LDL-cholesterol." C.A.J.A. 90381. At trial, Amarin's corporate representative confirmed that "Amarin had not yet conducted any clinical studies" on hypertriglyceridemia when it made these statements to FDA, which were "candid and truthful." C.A.J.A. 725, 721.

In 2009, Amarin continued relying on the prior-art Mori publication to promote Vascepa. C.A.J.A. 90860. In a partnering presentation, Amarin described Mori in a slide titled "EPA—No LDL Effect." C.A.J.A. 90904. Amarin's expert admitted that this presentation told Amarin's potential partner that Mori "teaches that 96 percent pure EPA, 4 grams per day, has zero percent change in LDL." C.A.J.A. 2626–2627. He also admitted that this "did not misrepresent Mori." *Ibid.*

In March 2010, still months before Amarin had its own data on hypertriglyceridemia, Amarin cited prior art to convince investors of a "Clear Differentiation between [Vascepa] and Lovaza." C.A.J.A. 90254. Amarin assured investors that Vascepa causes "[n]o DHA induced elevation" of LDL-C. *Ibid.* As proof, Amarin cited prior art—including Mori—in slides titled "Multiple Studies Demonstrate that DHA Raises LDL-C" and "Multiple Studies Demonstrate that EPA is LDL Neutral." C.A.J.A. 90256–90257. Amarin's trial witnesses confirmed that these statements were "accurate," "truthful," and did not "mischaracterize[]" the prior art. C.A.J.A. 709–710, 714–715, 2630.

Amarin did not obtain its own data on EPA's effects in severely hypertriglyceridemic patients until its "MARINE" study in late 2010, more than a year after filing its patent application. C.A.J.A. 2587.

Amarin published these results in an article recognizing that prior-art studies "suggested that purified EPA might reduce TG levels without increasing the LDL cholesterol levels" because, "although DHA treatment generally increased LDL cholesterol levels, EPA therapy did not." C.A.J.A. 90090, 90096. While the article states that the lack of LDL-C increases in MARINE was "unexpected" (C.A.J.A. 90096), its lead author, Bays, disagreed. Before the article was published, Amarin emailed Bays about adding the "unexpected" language, which was "very important for Amarin." C.A.J.A. 90055, 90070. Bays objected to this addition because stating that "this finding was 'unexpected' is in contradiction to the rest of the manuscript" and "largely guts * * * the reality of this drug development program." C.A.J.A. 90088.

Amarin kept relying on Mori even after launching Vascepa. In 2014, Amarin told FDA that "[t]he data from [Mori] support * * * that EPA and DHA have differential effects on other well-studied lipid parameters such as LDL-C." C.A.J.A. 94505–94506 & n.59.

D. Amarin mischaracterized prior art during prosecution, but the examiner still found the claims prima-facie obvious.

In February 2009, more than a year before Amarin had any data on EPA's effects in severely hypertriglyceridemic patients, Amarin filed a provisional patent application that ultimately issued as the six patents-in-suit. The patents' common specification contains no data. C.A.J.A. 73–207, 2593–2595. Instead, it recites laundry lists of possible clinical effects, including reductions in triglycerides and either no impact on, or a reduction in, LDL-C. C.A.J.A. 87–88 (5:15–7:44). The ten asserted claims, which recite

some of these possible clinical effects, all require the same method of treatment—administering 4 g/day of pure EPA for at least 12 weeks to a patient with triglycerides of at least 500 mg/dL. App. 46a.

The assigned examiner at the patent office repeatedly found these claims obvious. Among other references, the examiner cited a clinical trial by Hayashi, which taught the administration of EPA "to individuals with serum TG levels of 300 ± 233 mg/dl (i.e. between 67 mg/dl and 533 mg/dl)." C.A.J.A. 88683. Partly because these levels "overlap with the claimed ranges of serum TG," the examiner found "a *prima facie* case of obviousness." C.A.J.A. 88684. "Further, all the other variables claimed, like amount administered (4 g), period of treatment (12 weeks), purity of EPA-E (at least about 96%) are either similar or overlap with the data disclosed by the prior art," which Amarin did not dispute. C.A.J.A. 88685.

Amarin tried "to overcome the obviousness rejection" with secondary considerations, but they were "not sufficient." C.A.J.A. 88699. Given Hayashi, the examiner found that "[t]he prior art clearly teaches" the administration of pure EPA to "patients with TG levels * * * up to 530 mg/dl." *Ibid.* Amarin's secondary considerations were "not enough to overcome such a strong case of obviousness." C.A.J.A. 88700.

Undeterred, Amarin submitted a declaration from Phillip Lavin, a statistician. C.A.J.A. 88703–88706. Lavin declared that "not even one patient in [Hayashi] would be expected to have a TG level of 450 mg/dl or higher." C.A.J.A. 88704. Citing Lavin, Amarin argued to the examiner that "it is not reasonable for the [Patent] Office to allege that any of the subjects in Hayashi have baseline TG levels that overlap

with the presently claimed range." C.A.J.A. 87913. Amarin reasserted that "[e]ven if a *prima facie* case has been established," secondary considerations would rebut it. C.A.J.A. 87922.

In finally allowing the claims, the examiner accepted Lavin's opinion that "[t]he prior art does not teach the administration of ethyl-EPA to patients having TG levels between 500 and 1500 mg/dl (very high)." C.A.J.A. 88716. The examiner still found it "obvious to treat patients having TG above 500 mg/dl with 96% pure ethyl-EPA." *Id.* But now, without a finding that EPA was given to patients with severe hypertriglyceridemia, the examiner did not characterize his obviousness finding as "strong." Thus, Amarin "was able to overcome * * * obviousness" with alleged secondary considerations. C.A.J.A. 88717.

It is now beyond dispute that Lavin's statements to the patent office were false. At deposition, Lavin admitted that he would "rewrite" his declaration because "there must be at least one subject" with triglycerides above 500 mg/dL in Hayashi, and it is "likely that you have one or two observations above 533 [mg/dL]." App. 37a–38a. At trial, Amarin's expert did not "offer any type of statistical opinion to corroborate what Dr. Lavin told the patent office." App. 38a. And he admitted that four other prior-art studies on pure EPA, which the examiner overlooked, each had "at least one patient * * * with triglycerides over 500"—i.e., severe hypertriglyceridemia. C.A.J.A. 2656–2657; see also C.A.J.A. 1351–1355.

E. Based on a battle of experts at trial, the district court found clear and convincing evidence of obviousness.

After four years of litigation culminating in a seven-day trial, the district court issued a detailed opinion holding all asserted claims obvious. App. 3a–93a. Before reaching any conclusions regarding obviousness, the court recognized that it "must also consider whether objective indicia of non-obviousness support the Asserted Claims," and analyzed Amarin's evidence on that issue. App. 47a–59a. After reciting *Graham*'s four-factor test, the court recognized that respondents "bear the ultimate burden of proving, by clear and convincing evidence, that the Asserted Claims are invalid." App. 73a. The court also recognized that "it is not permissible to use hindsight * * * or to rely at all on the teachings of the claimed invention" to find obviousness. App. 44a–45a.

In evaluating the prior art, the district court found that Amarin "concede[d] a number of Defendants' key premises." App. 76a. "[T]here [wa]s no dispute that the only difference between the method in the Lovaza PDR and the method in the asserted claims is that Lovaza contained a mixture of EPA and DHA, instead of purified EPA." *Ibid.* "Nor [wa]s there any dispute that the increases in LDL-C caused by Lovaza were known, and that 'a skilled artisan would have been motivated to avoid LDL-C increases when treating patients with severe hypertriglyceridemia.'" *Ibid.* Citing Amarin's concessions, the court found that "a skilled artisan would have wanted to know which active ingredient in Lovaza—EPA or DHA—was responsible for the LDL-C increase (if not both), and that Mori addressed this exact issue." App. 77a. Amarin's expert "did not dispute that 'a

skilled artisan seeing that there's DHA and EPA in Lovaza, and seeing a side effect, would at least consider whether the side effect could be associated with only DHA or only EPA.'" *Ibid.* "Nor did he dispute that 'Mori found that the increase of LDL-C with DHA was statistically significant and the increase with EPA was not.'" *Ibid.* As the district court found, "the key premises that he conceded lead directly to the motivation to combine and reasonable expectation of success that Defendants have asserted." *Ibid.*

The court considered Amarin's counterarguments but found them "unavailing." App. 79a. It rejected Amarin's "factual premise that lacks evidentiary support—that patients with TG levels above 500 mg/dL respond differently to TG-lowering therapy than patients with TG levels below 500 mg/dL." App. 80a. Instead, the court credited expert testimony that "there is no 'magical mechanistic difference' between having triglycerides of 400, 500, or 600 mg/dL," and that "regardless of a patient's baseline triglycerides, 'the qualitative effects of medications * * * tend to be the same.'" App. 81a. Amarin's petition does not challenge any of these factual findings.

Emphasizing that it had not yet reached any final conclusion of obviousness, the court reiterated that "evidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness." *Ibid.* (quotation omitted). At trial, most of Amarin's secondary-considerations evidence focused on its "REDUCE-IT" study, which confirmed EPA's ability to reduce cardiovascular risk. App. 82a–88a. Amarin's amicus, Aimed Alliance, continues to rely extensively on this evidence (at 6–9, 11–14). The district court, however, found that REDUCE-IT lacks a nexus to

Amarin's claims—a finding that Amarin and its amici do not dispute. App. 82a–88a. The court also found that Amarin's claims are unsupported by unexpected results, skepticism, or praise—findings that are also no longer disputed. App. 88a, 90a–91a.

The only secondary considerations favoring Amarin were long-felt need, "weigh[ing] slightly in favor of" validity, and commercial success. App. 89a, 91a. But the district court did not (because it did not have to) consider whether Vascepa's purported success has a nexus to the claims. Overall, the district court found that Amarin's evidence of alleged secondary considerations was "weak." App. 92a.

At the end of its opinion, for the first time, the court reached its obviousness conclusion—"in view of all four *Graham* factors (including alleged secondary considerations), Defendants have proven by clear and convincing evidence that all Asserted Claims are invalid as obvious under 35 U.S.C. § 103." *Ibid.* Amarin's petition never mentions this conclusion.

F. The Federal Circuit summarily affirmed.

In a one-line order designated "nonprecedential," a three-judge panel of the Federal Circuit summarily affirmed the district court's decision after argument without opinion under local rule 36. App. 1a–2a.

Amarin filed a combined petition for panel rehearing and rehearing en banc, which was denied. App. 95a–96a. No judge voted to rehear the case or even called for a response to Amarin's petition.

REASONS TO DENY THE PETITION

I. The petition's "question presented" is not presented by the decisions below.

Certiorari should be denied, first, because the petition's question presented is not presented by either the Federal Circuit's decision or the district court's decision that it summarily affirmed. This case is thus an exceptionally poor vehicle to address the petition's question presented.

A. The Federal Circuit's decision does not implicate the question presented.

The Federal Circuit's decision is a one-line summary affirmance under local rule 36 that is unpublished and designated non-precedential. App. 1a–2a. It does not implicate any question at all, let alone the question presented or any "important question of federal law" worthy of review. Rule 10(c).

Amarin argues that this one-line order somehow "send[s] a clear signal that the misguided prima facie framework is the settled law of the circuit." Pet. 4. By definition, however, a summary affirmance does not "signal" anything. A rule 36 order "does not endorse or reject any specific part of the trial court's reasoning," "has no precedential value," and "cannot establish applicable Federal Circuit law." *Rates Tech., Inc.* v. *Mediatrix Telecom*, 688 F.3d 742, 750 (Fed. Cir. 2012). The Federal Circuit issues such orders when a trial court's decision "is based on findings that are not clearly erroneous" and "an opinion would have no precedential value." Fed. Cir. R. 36(a)(1). As with other nonprecedential decisions, rule 36 orders do "not add[] significantly to the body of law" and do not have "the effect of binding precedent." Fed. Cir. R. 32.1(b), (d). Regardless of the

merits, therefore, the decision below will have no impact on any other case. Amarin's request for error correction in this single case does not warrant the Court's review.

Aware of this difficulty, Amarin urges the Court to "vacate and remand * * * so that the Federal Circuit can further consider whether Amarin's invention is obvious." Pet. 31. But that kind of micromanagement is not a proper use of this Court's certiorari jurisdiction. "[W]hether Amarin's invention is obvious"—the only question actually presented by the decisions below—is a narrow, fact-specific issue that has no bearing on other parties or cases. Nor does Amarin allege anything improper about the Federal Circuit's use of summary affirmances, which this Court has repeatedly declined to review.[2] Indeed, appellate courts "have wide latitude in their decisions of whether or how to write opinions. That is especially true with respect to summary affirmances." *Taylor* v. *McKeithen*, 407 U.S. 191, 194 n.4 (1972).

In short, the one-line order below does not implicate any issue that warrants this Court's review. For this reason alone, certiorari should be denied.

B. The district court's decision does not implicate the question presented.

The district court's decision also does not implicate the question presented. Its lengthy opinion, issued after a seven-day trial, does not purport to make

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[2] See, *e.g.*, *Fote* v. *Iancu*, 140 S. Ct. 2765 (2020) (No. 19-1129); *Kaneka Corp.* v. *Xiamen Kingdomway Grp.*, 140 S. Ct. 2768 (2020) (No. 19-1228); *Specialty Fertilizer Prods., LLC* v. *Shell Oil Co.*, 138 S. Ct. 2678 (2018) (No. 17-1243); *Shore* v. *Lee*, 137 S. Ct. 2197 (2017) (No. 16-1240).

new law or even address any dispute about legal standards. Rather, the opinion is intensely factual and turns on detailed findings specific to Amarin's patents. App. 3a–93a.

Arguing otherwise, Amarin mischaracterizes the district court's decision, which did not "fail[] to consider objective indicia along with the other factors." Pet. 26. The court expressly considered "all four *Graham* factors" together: "For the reasons discussed above, *in view of all four Graham factors (including alleged secondary considerations)*, Defendants have proven by clear and convincing evidence that all Asserted Claims are invalid as obvious under 35 U.S.C. § 103." App. 92a (emphasis added). Amarin never cites this conclusion.

Nor does Amarin cite the court's repeated acknowledgments that the "obviousness inquiry must also consider whether objective indicia of non-obviousness support the Asserted Claims," that "evidence rising out of the so-called 'secondary considerations' must always when present be considered en route to a determination of obviousness," and that respondents "bear the ultimate burden of proving, by clear and convincing evidence, that the Asserted Claims are invalid." App. 47a, 73a, 81a (quotations omitted). These are the same legal standards that Amarin asks this Court to uphold. The district court even quoted Amarin's cited authorities for these principles, including *Graham* and *Stratoflex, Inc.* v. *Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983). App. 47a, 81a; Pet. 21. Even if the court had misapplied those standards or improperly weighed the evidence (which it did not), certiorari would not be appropriate to correct "erroneous factual findings or misapplication of a properly stated rule of law." Rule 10.

That "the district court first determined that [respondents] 'presented clear and convincing evidence at Trial that all Asserted Claims are invalid as obvious'" (Pet. 14) does not imply that it shifted the burden of proof to Amarin on secondary considerations. As Amarin acknowledges, the "party challenging patent validity bears "a heavy burden of persuasion, requiring proof by clear and convincing evidence." Pet. 23 (quoting *Microsoft Corp.* v. *i4i Ltd. P'ship*, 564 U.S. 91, 95, 102 (2011) (alteration omitted)). Thus, if respondents had not presented such evidence at the outset, their obviousness challenge would have failed *regardless* of secondary considerations. Indeed, where a challenger "fail[s] to establish obviousness by clear and convincing evidence," the court "need not address [the] evidence of objective indicia of nonobviousness." *ProBatter Sports, LLC* v. *Sports Tutor, Inc.*, 680 F. App'x 972, 976 (Fed. Cir. 2017).

Moreover, although the district court found "clear and convincing *evidence*" of obviousness, it reserved its *conclusion* of obviousness until after reviewing "all four *Graham* factors." App. 76a, 92a (emphasis added). "Despite the phrasing employed," therefore, "it is clear that the district court did consider the objective indicia before reaching its ultimate obviousness conclusion." *PAR Pharm., Inc.* v. *TWI Pharm., Inc.*, 773 F.3d 1186, 1199 (Fed. Cir. 2014). Because the district court did, in fact, consider "all four *Graham* factors" in finding Amarin's patents obvious (App. 92a), its decision does not implicate the question presented, which does not merit this Court's review.

II. Answering the question presented in Amarin's favor would not change the outcome.

Even if the petition's question presented were raised by either decision below (it is not), this case would still be an exceptionally poor vehicle because answering that question in Amarin's favor would not affect the outcome of the case. Amarin outright ignores the district court's factual findings on the first three *Graham* factors, selectively focuses on some of the court's findings on secondary considerations, and ignores the court's other findings on secondary considerations that were unfavorable to Amarin. The evidence at trial overwhelmingly showed that the treatment method claimed by Amarin's patents was obvious, and no amount of "long-felt need" or "commercial success" could show otherwise. Moreover, the evidence was undisputed that the alleged "commercial success" of Vascepa does not result from Amarin's patented invention. Thus, even if that success were given greater weight, it would not affect the outcome because Amarin's patents are invalid either way.

A. The claims are obvious regardless of how secondary considerations are weighed.

This was not a close case. As the district court found, "the key premises that [Amarin's own expert] conceded lead directly to the motivation to combine and reasonable expectation of success that Defendants have asserted"—a factual finding that Amarin and its amici no longer dispute. App. 77a. On the other side of the ledger, the court found that, "at best," there was only "weak evidence of * * * secondary considerations." App. 92a. In particular, only "commercial success" and a "slight[]" showing of "long-felt need" favored validity. App. 91a, 89a. As

Amarin admits, "[t]he district court disagreed with Amarin about other objective indicia, such as unexpected benefits, initial industry skepticism, and ultimate praise," and Amarin has abandoned any challenge to these factual findings. Pet. 15.

The undisputed facts compel a finding of obviousness regardless of how Amarin's evidence of commercial success and long-felt need are weighed. This Court has repeatedly held that these secondary considerations, without more, cannot overcome a strong case of obviousness. As the Court made clear in a passage quoted by Amarin itself, such secondary indicia will "'tip the scales in favor of patentability'" only "'in a close case.'" Pet. 21 (quoting *Goodyear Tire & Rubber Co.* v. *Ray-O-Vac Co.*, 321 U.S. 275, 279 (1944)). Indeed, that was the holding in *Graham* itself: "[T]he long-felt need in the industry for [the claimed invention] together with its wide commercial success supports its patentability. * * * However, these factors do not, in the circumstances of this case, tip the scales of patentability." *Graham*, 383 U.S. at 35–36. The same is true here—given the strong (and now undisputed) evidence of obviousness, secondary considerations cannot "tip the scales."

Graham's holding is consistent with this Court's other cases that have found secondary considerations insufficient to overcome a strong case of obviousness. In *Sakraida* v. *Ag Pro, Inc.*, for example, the Court held that a claimed invention "would be obvious to any person skilled in the art" despite "enjoying commercial success." 425 U.S. 273, 282 (1976). Likewise, in *Great Atlantic & Pacific Tea Co.* v. *Supermarket Equipment Corp.*, the Court found a patented invention obvious despite "evidence that th[e] [claimed] device filled a long-felt want and has enjoyed commer-

cial success." 340 U.S. 147, 153 (1950). The same was true in *Dow Chemical*, where the patentee also relied on "long felt want" and "commercial success." 324 U.S. at 330. As the Court made clear, "these considerations are relevant only in a close case where all other proof leaves the question of invention in doubt"—not where, as here, "the lack of invention is beyond doubt and cannot be outweighed by such factors." *Ibid.* The Court reached a similar result in *Jungersen* v. *Ostby & Barton Co.*, where "[t]he fact that th[e] [claimed] process has enjoyed considerable commercial success, however, d[id] not render the patent valid." 335 U.S. 560, 567 (1949). Amarin does not cite, much less distinguish, any of these cases.

Because Amarin's patents would remain obvious regardless of how much weight commercial success and long-felt need are given, this case is a poor vehicle to address their role in an obviousness analysis. The Court should deny Amarin's petition.

B. Vascepa's alleged commercial success lacks a nexus to the claims.

Certiorari should also be denied because Vascepa's alleged commercial success does not result from the patents-in-suit. It is well established, and Amarin does not dispute, that "for commercial success to be probative evidence of nonobviousness, a nexus must be shown between the claimed invention and the evidence of commercial success." *Wm. Wrigley Jr. Co.* v. *Cadbury Adams USA LLC*, 683 F.3d 1356, 1363 (Fed. Cir. 2012). Where "the evidence does not show that the success of [a] product was directly attributable to" the claimed invention, the product's commercial success must be "discounted." *Id.* at 1364. Here, undis-

puted evidence shows that Vascepa's alleged success does *not* result from the patented invention.

At trial, Amarin's economic expert admitted that only "one-third of the sales of Vascepa, from 2013 to 2018, related to patients with severe hypertriglyceridemia"—the population covered by Amarin's patents. C.A.J.A. 2195. By 2018, only "25 percent of the sales of Vascepa related to patients that have TG levels of 500 or more." *Ibid.*; see also C.A.J.A. 108947. Similarly, Amarin's clinical expert admitted that "85 percent of [his Vascepa] patients did not ever have triglycerides above 500," which Amarin's asserted patents expressly require. C.A.J.A. 1055–1056.

Because the district court found such strong evidence of obviousness, it did not need to address the issue of nexus. Nevertheless, the lack of any nexus between Vascepa's sales and Amarin's patents is an alternative ground for affirmance, which makes this case particularly ill-suited to evaluate the impact of commercial success in an obviousness case.

III. The decisions below are correct and do not conflict with any precedent.

Even if the decisions below implicated the question presented (they do not), and even if that question could affect the outcome (it could not), certiorari would still be unwarranted because the "prima facie framework" that Amarin purports to challenge is consistent with both this Court's and the Federal Circuit's precedent. There is no conflict to resolve.

A. There is no conflict with this Court's precedent.

Nothing in this Court's precedent precludes making an initial determination of obviousness and then

evaluating whether secondary considerations overcome that determination. That is exactly what this Court did in *KSR* by first holding that "[t]he prior art discussed above leads us to the conclusion that [the claimed invention] would have been obvious," and *then* holding that the patentee "has shown no secondary factors to dislodge the determination that [the invention] is obvious." 550 U.S. at 425–426. Amarin's position cannot be reconciled with *KSR*, where this Court used the same "framework" to address secondary considerations that Amarin now challenges. Not surprisingly, since *KSR*, this Court has repeatedly denied petitions with questions presented that are nearly identical to Amarin's. See *Cubist Pharm., Inc.* v. *Hospira, Inc.*, 136 S. Ct. 2393 (2016) (No. 15-1210); *B/E Aerospace, Inc.* v. *C&D Zodiac, Inc.*, 139 S. Ct. 55 (2018) (No. 17-1252); *ZUP, LLC* v. *Nash Mfg., Inc.*, 139 S. Ct. 1211 (2019) (No. 18-823).

Amarin argues that it is improper to "relegate[] objective indicia of nonobviousness to a *secondary* role" (Pet i), but this Court expressly labeled them "*secondary* considerations" in *Graham*, 383 U.S. at 17, and "*secondary* factors" in *KSR*, 550 U.S. at 426 (emphases added). These "secondary" indicia "*might* be utilized" and "*may* have relevancy" in some cases, but they have never taken center stage. *Graham*, 383 U.S. at 17–18 (emphases added). Again, they "tip the scales" only "in a close case." *Goodyear Tire*, 321 U.S. at 279; *Dow Chem.*, 324 U.S. at 330.

Equally misguided is Amarin's argument that the district court erred by addressing secondary considerations only after its analysis of the prior art. According to Amarin, *KSR* "explained that 'the sequence of the[] questions' posed by the four *Graham* factors 'might be reordered in any particular case,' meaning

no one factor need be considered first or last." Pet. 7. Yet this argument is waived: Before the district court, Amarin itself addressed secondary considerations last, in a section titled "Objective Indicia *Reinforce* the Non-Obviousness of the Asserted Claims." Pet. D.C. Post-Trial Br. 25 (emphasis added).

In any event, Amarin's argument turns *KSR* on its head. At most, *KSR* leaves the order of certain *Graham* factors to the court's discretion; it does not *prevent* courts from addressing secondary considerations last. That prohibition would impose the same type of "rigid rule" that *KSR* rejected and, indeed, would contradict *KSR* itself, which expressly addressed "secondary factors" last. 550 U.S. at 419, 426. Tellingly, Amarin does not cite a single case that did *not* address secondary considerations last. The district court's treatment of secondary considerations was entirely consistent with this Court's precedent.

B. There is no conflict with the Federal Circuit's precedent.

Amarin also fails to show any relevant conflict within the Federal Circuit. It relies extensively on Judge Reyna's dissent in *Intercontinental Great Brands*, 869 F.3d 1336 (Pet. 2–3, 22–24), but ignores that Judge Reyna was on the panel below, which voted unanimously to affirm. Indeed, this case is analogous to another unanimous decision by Judge Reyna that came after *Intercontinental* and rejected Amarin's same arguments: "While the district court's discussion of objective indicia follows its discussion of the asserted prior art, the substance of the court's analysis makes clear that it properly considered the totality of the obviousness evidence." *Persion Pharm. LLC* v. *Alvogen Malta Operations Ltd.*, 945 F.3d

1184, 1194 (Fed. Cir. 2019) (Reyna, J., joined by O'Malley, J., and Chen, J.). The same is true here.

Amarin argues that "[t]he Court should grant certiorari to hold that *Graham*'s totality of the evidence framework governs" (Pet. 27), but that standard *already* governs, as the en banc Federal Circuit has made abundantly clear: "A determination of whether a patent claim is invalid as obvious under § 103 requires consideration of all four *Graham* factors, and it is error to reach a conclusion of obviousness until all those factors are considered." *Apple Inc.* v. *Samsung Elecs. Co.*, 839 F.3d 1034, 1048 (Fed. Cir. 2016) (en banc). This Court's intervention is not needed.

Whether some courts refer to a "prima facie" case when summarizing their findings on the first three *Graham* factors is a question of semantics, not substance. Indeed, that is what Amarin itself told the court below—and any argument to the contrary is now waived. Although Amarin challenged the district court's obviousness analysis, it made clear that "[n]one of this is to say that a district court commits error whenever it utters the words 'prima facie case' in conducting an obviousness analysis." C.A. Opening Br. 44. In fact, Amarin expressly "recognized that *a court may correctly analyze obviousness utilizing a framework that looks to a 'prima facie' case and then to objective indicia*—provided that the court withholds its conclusion until considering the objective indicia." C.A. Reply Br. 3 (emphasis added).

That is consistent with the cases that Amarin endorses as "be[ing] on the right track," including *In re Cyclobenzaprine* (Pet. 21–22), which explains that "even panels that have used the 'prima facie' and 'rebuttal' language generally have made clear that a

fact finder must consider *all* evidence of obviousness and nonobviousness before reaching a determination." 676 F.3d at 1077. Amarin's purported distinction between purported "prima facie" and "totality" "frameworks" is thus semantic and reflects no substantive conflict.

Finally, in passing, Amarin suggests that the district court's decision conflicts with *Miles Labs., Inc.* v. *Shandon Inc.*, 997 F.2d 870, 878 (Fed. Cir. 1993), because it "weighed the objective indicia it found *against* other objective indicia it found were not proven." Pet. 26. Yet the district court did no such thing. Amarin takes a single sentence out of context, ignoring the court's earlier, explicit findings that Amarin's alleged evidence of unexpected results, skepticism, and praise "does not weigh in favor of * * * nonobvious[ness]." App. 88a, 91a. Again, Amarin does not dispute these factual findings. The district court's exhaustive, fact-intensive analysis of secondary considerations does not merit this Court's review.

CONCLUSION

For the foregoing reasons, the petition for a writ of certiorari should be denied.

Respectfully submitted.

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