

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

REPLY BRIEF FOR PETITIONERS

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INTRODUCTION

Amarin invested heavily to develop VASCEPA®—its only drug on the market. No one had developed a treatment for severe hypertriglyceridemia that does not raise harmful LDL-C before Amarin, and yet the lower courts found Amarin’s invention obvious by viewing the prior art in hindsight. That erroneous framework hinders research and innovation, as amici explained. The Court should grant certiorari, hold that *Graham*’s totality framework governs, and restore proper incentives for innovation. *See Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966).

Respondents’ opposition misunderstands the totality framework this Court prescribed. Respondents repeatedly point to the district court’s statement that it found obviousness “in view of all four *Graham* factors” (Pet. App. 92a), which they argue shows a totality analysis. But the problem with the district court’s decision, as Amarin explained, is that it found prima facie obviousness based solely on *Graham*’s technical factors and only then turned to objective indicia to ask if they rebutted that finding. As dissenting Federal Circuit judges have explained, such two-tiered analysis artificially diminishes the weight accorded to objective indicia and incorrectly shifts the burden to the patentee to show nonobviousness. By contrast, *Graham*’s totality framework requires consideration of all four factors together *before* making any obviousness determination, so that objective indicia can effectively guard against hindsight bias.

Respondents assert that *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), blessed the prima facie approach, but *KSR* did not even mention the prima facie framework, and objective indicia were not at issue

in that case. To the extent the Court in *KSR* stated that the prior art supported obviousness and the objective indicia did not dislodge that conclusion, that was only because the Court was considering (and invalidating) a test that concerned the technical factors. After all, *KSR* noted that any one *Graham* factor may be considered first, rejecting a mode of analysis that (like the prima facie framework) always considers objective indicia last. And although respondents contend there is no conflict within the Federal Circuit, Amarin never argued an intra-circuit conflict. As Amarin explained, the Federal Circuit has now *settled* on the prima facie framework, which reinforces the need for this Court's review.

None of respondents' purported vehicle issues presents an obstacle to certiorari. While respondents argue (Opp. 1) that the Federal Circuit's summary affirmance "does not raise any issue at all," this Court has reviewed summary-affirmance cases, including recently a Rule 36 judgment. *See* Pet. 30. Similarly, the district court's factual findings, including its statement that the evidence of objective indicia was "weak" (Pet. App. 92a), have little relevance at this stage. The proper *Graham* framework is a threshold legal issue in any obviousness inquiry and the only question presented here. If the Court holds that the lower courts applied an incorrect framework, the remaining factual questions are for the lower courts to decide on remand. Moreover, the district court found objective indicia weak because it viewed them through the wrong legal lens and allowed some of those indicia to undermine others, all pursuant to the erroneous prima facie framework.

ARGUMENT

I. THE FEDERAL CIRCUIT'S PRIMA FACIE FRAMEWORK CONFLICTS WITH THIS COURT'S PRECEDENT

Respondents argue that the prima facie framework is “consistent with both this Court’s and the Federal Circuit’s precedent.” Opp. 25. But *Graham*, *KSR*, and other decisions of this Court require consideration of all *Graham* factors together before reaching any obviousness conclusion, instead of making a prima facie obviousness determination based solely on the technical factors and then considering objective indicia merely as rebuttal. Pet. 18-21. The fact that the Federal Circuit has now decided to consistently authorize the prima facie framework *supports* certiorari, because it shows that the erroneous legal framework is here to stay absent this Court’s intervention.

A. Respondents argue that objective indicia may be relegated to a second tier because the Court in *Graham* called them “secondary considerations” that “might be utilized” and “may have relevancy.” Opp. 26 (emphases omitted). But the reference to “secondary” is not prescriptive. To the contrary, the Court emphasized that objective indicia can play an important role that no other *Graham* factor can: they “guard against slipping into use of hindsight” and “resist the temptation to read into the prior art the teachings of the invention in issue.” *Graham*, 383 U.S. at 36. And while objective indicia obviously play no role when they are not present, and may be more or less important depending on the strength of the evidence, none of that suggests that, where present, objective indicia are subsidiary to the technical factors, as the Federal Circuit now holds.

Likewise, this Court’s observation that objective indicia “should, in a close case, tip the scales in favor of

patentability,” *Goodyear Tire & Rubber Co. v. Ray-O-Vac Co.*, 321 U.S. 275, 279 (1944) (quoted at Opp. 26), does not diminish the relative importance of objective indicia. As the Court explained in *Graham*, objective indicia “give light to the circumstances surrounding the origin” of the invention, including the technical factors. 383 U.S. at 17-18. In an ordinary case, therefore, objective indicia may illuminate whether the technical factors in fact present “a close case.” *Graham*’s totality framework ensures a fair shake to objective indicia so that they *can* tip the scales in favor of nonobviousness in an appropriate case. Pet. 19-21. The prima facie framework, by contrast, systematically disadvantages objective indicia by limiting their role to rebuttal and all but ensures that they will not matter. Pet. 22-24. Indeed, the Federal Circuit has “rarely held” that evidence of objective indicia is “extensive” and thus “sufficient to overcome a prima facie case of obviousness.” *Transocean Offshore Deepwater Drilling, Inc. v. Maersk Drilling USA, Inc.*, 699 F.3d 1340, 1354 (Fed. Cir. 2012); *see also Ohio Willow Wood Co. v. Alps South, LLC*, 735 F.3d 1333, 1344 (Fed. Cir. 2013).

KSR confirms the distinction between the totality framework that *Graham* requires and the prima facie framework that the Federal Circuit has now imposed. Although the Court in *KSR* explained that the “the sequence of the[] questions” posed by *Graham*’s four factors may be “reordered” in any given case, 550 U.S. at 399, the prima facie framework predetermines that objective indicia will be considered last and only to rebut an obviousness determination already made. Respondents misunderstand that fundamental incompatibility. *See* Opp. 27. Even within the totality framework, courts may well consider objective indicia last. What contravenes this Court’s precedent is a two-tiered in-

quiry that determines prima facie obviousness first, before considering any objective indicia invariably as the last step.¹

Contrary to respondents' argument (Opp. 26), *KSR* did not apply "the same 'framework'" as the Federal Circuit now requires. As an initial matter, *KSR* nowhere mentions a prima facie framework. The question there was whether the Federal Circuit may employ a rigid "'teaching, suggestion, or motivation' test (TSM test)" that required motivation or suggestion derived in part from the technical factors to show obviousness. 550 U.S. at 407. The Court invalidated that test and instead addressed the technical factors more holistically, which supported obviousness. *Id.* at 415, 422-426. The Court then stated that "[l]ike the District Court," it concluded that the patent licensee had "shown no secondary factors to dislodge" its obviousness determination. *Id.* at 426.

The Court's phrasing in no way opined on—much less minimized—the role of objective indicia, which were not at issue in *KSR*. Rather, the opinion's wording reflected the fact that it reviewed and invalidated the TSM test, which concerned the technical factors. The Court thus focused on those factors in order to show how they should be considered instead of the TSM test. The statement regarding objective indicia merely agreed with the district court that there were no valid objective indicia, an observation necessary to find obviousness (*see* Opp. 28). The Court nowhere authorized the Federal Circuit's prima facie framework, especially given that the Court warned against hind-

¹ For similar reasons, respondents' argument (Opp. 27) that Amarin waived its *KSR* argument by listing objective indicia last in its district court post-trial briefing is meritless.

sight bias and explained that any one *Graham* factor may be considered first. *See* 550 U.S. at 407, 421.

B. Respondents argue bizarrely there is no “relevant conflict within the Federal Circuit.” Opp. 27. But that is just the problem—despite well-founded misgivings about the prima facie framework years ago, the Federal Circuit has now made up its mind and the prima facie framework has become the rule. Pet. 21-24.

Contrary to respondents’ view, the difference between the prima facie framework and the totality framework is not just “semantic” (Opp. 28-29).² Respondents do not appear to dispute that the legal framework affects the outcome of the analysis or that the prima facie framework leads to over-invalidation of patents. *See* Pet. 28-30. In any event, the fact that this Court has found patentability based on objective indicia in prior cases (Pet. 19-21), whereas the Federal Circuit (by its own admission) rarely has, shows how consequential the prima facie framework can be in an obviousness inquiry.

II. THIS CASE PLAINLY RAISES THE QUESTION PRESENTED

A. This case undoubtedly presents the permissibility of the prima facie framework. The district court was first “persuaded” of prima facie obviousness based solely on the technical factors; only then did it turn to objective indicia to see if they rebutted that determina-

² Contrary to respondents’ assertion (Opp. 28), Amarin did not agree that the use of a prima facie framework is “a question of semantics, not substance.” What Amarin noted is that courts could follow *Graham*’s framework where they consider all factors before making any obviousness determination, even if they nominally use the language of a prima facie case. *See* C.A. Opening Br. 44-45; C.A. Reply Br. 3. That is not what the district court did here.

tion. Pet. App. 75a-76a, 81a; *see* Pet. 14-15. In fact, it could not have been clearer that the district court addressed objective indicia *separately* from the technical factors—contrary to *Graham*’s totality framework—because the court found that VASCEPA’s satisfaction of a long-felt but unmet need and commercial success were “outweighed by” certain “other proffered secondary considerations.” Pet. App. 92a. Plainly, the court considered objective indicia to be a category unto themselves wherein different considerations may undermine each other, rather than each objective consideration directly contributing to the overall obviousness determination as other *Graham* factors would. Pet. 26-27.

Respondents assert (Opp. 21) that the district court applied *Graham*’s totality framework because it “reserved its *conclusion* of obviousness until after reviewing ‘all four *Graham* factors,’” but the district court’s decision contradicts that view. The court’s concluding statement that Amarin’s invention was obvious “in view of all four *Graham* factors” (Pet. App. 92a) does not refute the district court’s adherence to the prima facie framework. The court determined that Amarin’s invention was prima facie obvious based solely on *Graham*’s technical factors, and then found that the objective indicia did not rebut that determination, resulting in the very problems that dissenting Federal Circuit judges have identified. *See* Pet. 22-24. Those are not “the same legal standards that Amarin asks this Court to uphold.” Opp. 20.

B. Respondents’ broad assertion (Opp. 18) that the Federal Circuit’s Rule 36 judgment “does not implicate any question at all” is untenable. By that standard, the Federal Circuit could insulate its decisions from this Court’s review simply by issuing summary affirmances,

which it does in about 30% of its cases. *See* Pet. 30-31. Understandably, the Court has not adopted such a categorical rule, having granted review in summary-affirmance cases including where the Federal Circuit issued a Rule 36 judgment (*see* Pet. 30)—none of which respondents address. And respondents’ related argument (Opp. 18) that summary affirmance cannot “‘signal’ anything” because it is not precedential has it backwards. As Amarin explained (Pet. 30), the Federal Circuit’s apparent belief that its decision would have “no precedential value,” Fed. Cir. R. 36(a), shows that the court will not revisit the permissibility of the prima facie framework on its own, thus confirming that the issue is ripe for this Court’s intervention.

There is nothing objectionable about Amarin’s “vacate and remand” request either. In the event the Court determines that the lack of a Federal Circuit opinion somehow presents an obstacle to granting review, the Court should vacate and remand with instructions on *Graham*’s totality framework. Pet. 31. That alternative request is no more “micromanagement” (Opp. 19) than what this Court has done in prior cases. Pet. 31 (citing cases).

III. THE REMAINING ISSUES ARE FOR LOWER COURTS TO DECIDE

Respondents contend that applying *Graham*’s totality framework would not change the outcome because the district court made various factual findings that respondents believe would support obviousness at any rate. Opp. 22-25. In the first place, the existence of factual issues is no ground to deny review. If the Court holds the prima facie framework impermissible (a threshold legal issue and the only question presented here), it is for the lower courts to apply the proper

framework on remand, including by revising any factual findings as appropriate.³ It makes particularly little sense for certiorari to depend on a factual issue that the district court (or the Federal Circuit) did not address, such as whether VASCEPA's commercial success lacked nexus to the patent claims. Opp. 24-25.

In any event, respondents are wrong on the merits. Respondents argue (Opp. 22-24) that this was not a close case because the district court found that the technical factors supported obviousness and deemed objective indicia to be "weak" (Pet. App. 92a). But the court's conclusion that the prior art supported obviousness was possible only by viewing the prior art in hindsight without regard for objective indicia. For instance, the objective evidence showed that no one had developed a treatment for severe hypertriglyceridemia that does not raise LDL-C, despite the asserted prior art teachings. Pet. 25-26. Moreover, the court concluded that objective indicia were "weak" only because it allowed its *prima facie* obviousness finding to devalue objective indicia. For example, the court found that the long-felt but unmet need for VASCEPA only "slightly" favored nonobviousness because the improvement that Amarin's invention represented was "*a prima facie obvious one.*" Pet. App. 89a (emphasis added). The court then exacerbated the problem by allowing objective indicia to cancel each other out. Pet. App. 88a-92a. Respondents' argument (Opp. 29) that the district court's statement adopting that approach is "a single sentence out of context" is flatly wrong. Under the heading "Weighing These Secondary Considerations," the court

³ Just because Amarin seeks review of the *prima facie* framework does not mean it "abandoned" (Opp. 22-23) other arguments that may be relevant on remand.

stated that the objective indicia it found were “outweighed” by “other proffered secondary considerations” that it disagreed with and “[t]hus, at best, [Amarin] ha[s] presented weak evidence of the existence of secondary considerations, which do not overcome the Court’s finding that all Asserted Claims are prima facie obvious.” Pet. App. 91a-92a. The “context” speaks for itself.⁴

There is also no basis to discount VASCEPA’s commercial success. *See* Opp. 24-25. If anything, the fact that a large portion of VASCEPA’s sales comes

⁴ Respondents’ Statement is replete with one-sided and often misleading characterizations of the record. For example, although respondents state (Opp. 8, 14) that “at least five prior-art studies on pure EPA included patients with” severe hypertriglyceridemia, none involved *populations* with severe hypertriglyceridemia. They were thus inadequate to form conclusions about EPA’s effects on those populations, as respondents’ own expert admitted. C.A.J.A. 1398-1399. Respondents’ focus on Lavin’s declaration (Opp. 13-14) is likewise a distraction. The Examiner did not rely on his declaration (C.A.J.A. 88046-88053), and respondents’ expert admitted that Hayashi—the subject of Lavin’s declaration—was “not telling us anything about the effect of EPA on LDL-C values in severely hypertriglyceridemic patients” (C.A.J.A. 1493-1494). Respondents also rely on an email from Dr. Bays to argue that the results of Amarin’s clinical trial (the MARINE study) were not unexpected (Opp. 12), contrary to a statement in Dr. Bays’s own published article that the results *were* unexpected (C.A.J.A. 90096). But Dr. Bays testified that he was unsure of what he meant in the email, which predated his peer-reviewed article, because his “expectation was, prior to getting the results of the MARINE trial ... that the LDL cholesterol levels would rise after administration of [EPA] in patients with very high triglyceride levels” (C.A.J.A. 3437-3439, 3445-3447, 48679). Finally, none of Amarin’s supposed “concessions” (Opp. 15-16) changes the key point that there was no reasonable expectation of success that EPA would avoid LDL-C increase in patients with severe hypertriglyceridemia, which respondents were required to prove to establish obviousness.

from patients with triglyceride levels below 500 mg/dL (i.e., not “very high” or “severe”) supports nonobviousness. As Amarin explained below, healthcare providers typically have the option, based on their medical judgment, to prescribe drugs that (like VASCEPA) treat very high levels of triglycerides to patients with lower triglyceride levels. C.A.J.A. 103303. Had Amarin’s invention been obvious, other pharmaceutical companies would have been induced to bring a drug like VASCEPA to market sooner because of the potential for considerable sales to patients with very high *and* lower triglyceride levels. *Id.* But they did not. In any event, even VASCEPA’s net sales to only those patients with severe hypertriglyceridemia have increased sixfold since VASCEPA’s launch, further supporting the nexus between VASCEPA’s commercial success and the asserted claims. C.A.J.A. 103303, 2189.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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