No. 09-117

In the Supreme Court of the United States

APOTEX, INC. and APOTEX CORP.,

Petitioners,

v.

SANOFI-SYNTHELABO, SANOFI-SYNTHELABO INC., and BRISTOL-MYERS SQUIBB SANOFI PHARMACEUTICALS HOLDING PARTNERSHIP,

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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RULE 29.6 STATEMENT

Petitioners hereby incorporate by reference the statement pursuant to Rule 29.6 included in the petition for a writ of certiorari.

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REPLY BRIEF FOR PETITIONERS

In making so much of the supposedly unpredictable aspects of the chemistry at issue, respondents ("Sanofi") advance in this Court the very legal proposition that petitioners ("Apotex") contend is erroneous and warrants further review. Ultimately respondents fail to grapple with petitioners' basic point: An obsessive focus on *outcomes* rather than the *obviousness of the path followed to reach a result* is starkly inconsistent with the approaches of the U.S. Patent and Trademark Office and other courts of appeals in an earlier era; contrary to sound patent policy; and in conflict with a century of this Court's case law culminating in *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398 (2007).

Respondents' lengthy brief seems concerned more than anything with calling attention to the sweat of Sanofi's brow. That sweat, however, is legally immaterial. It was already rewarded, moreover, with a valid earlier patent against which the later one at issue must be judged. The petition raises a recurring issue of profound importance, and it should be granted so this Court can clarify that *KSR*'s lessons apply with no less force in an "unpredictable art."[1]

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[1] Respondents point out that the PTO has agreed to conduct a reexamination proceeding for the '265 patent. BIO 18. In the past this Court has been entirely untroubled by the pendency of such a proceeding. See *eBay Inc.* v. *MercExchange L.L.C.*, 547 U.S. 388, 391 n.1 (2006). In this case, even if the PTO were to invalidate the '265 patent, a final decision to that effect would not issue for many years.

I. Respondents Defend the Erroneous View of the Courts Below That Any Element of Unpredictability Is Sufficient To Confer Patentability Even If an Approach Was "Obvious To Try."

A. Respondents halfheartedly say that Apotex is "unfair[]" to characterize the Federal Circuit's decision as saying that any aspect of unpredictability in an experiment is sufficient to patent the result. Br. in Opp. ("BIO") 26. But the district court clearly believed that "evidence of the fact that *any* property of clopidogrel bisulfate is unexpected . . . rebuts the *presumption that clopidogrel bisulfate is obvious*," Pet. App. 107a (emphasis added), and respondents defend the court's "conclu[sion] that *each*" one of the compound's supposedly unexpected properties "rebutted that prima facie case," BIO 16 (emphasis added).

The Federal Circuit obviously agreed. It is respondents who repeatedly call attention (BIO 16, 20, 26) to its justification for affirming: "[A] person of ordinary skill would not have had the *expectation* that separating the enantiomers would be *likely* to produce an isomer having [i] absolute stereoselectivity as to *both* [ii] the favorable antiplatelet activity *and* [iii] the unfavorable neurotoxicity." Pet App. 30a (emphasis and bracketed numbers added). In other words, a person of ordinary skill would not have bet all his chips on the precise eventual outcome, even though it was (as Sanofi concedes, BIO 6) within the known range of possible outcomes, see Pet. 4, and (as Sanofi does not really dispute, see BIO 8) there were good, *objective* reasons why someone would want to separate the enantiomers of PCR4099. See Pet. 16; Br. of *Amici Curiae* AARP et

al. 6. In requiring a demonstration that the *exact* outcome would have seemed "likely" – and not just within a likely *range* of desirable results motivating the experiment – the Federal Circuit set the bar for a § 103 challenge far too high.

Yet respondents have followed suit. They contend that "predictability [i]s an essential attribute" of obviousness. BIO 19. If (as respondents contend) predictability is *necessary* to invalidate a patent under § 103, then the contrapositive is also true: unpredictability – *any* unpredictability beyond the *de minimis* – must be sufficient to uphold it. Respondents and the Federal Circuit are both saying the same – erroneous – thing.

B. Respondents and the Federal Circuit have disregarded established legal principles. The petition explained that the proposition they advance – that an unexpected result trumps the obviousness of the path followed to reach it – clashes with this Court's prior decisions and with court of appeals decisions from before the creation of the Federal Circuit. Pet. 14-15; see, *e.g.*, *Ansonia Brass & Copper Co.* v. *Elec. Supply Co.*, 144 U.S. 11, 18 (1892) (the "application of an old process to a new and analogous purpose does not involve invention, even if the new result had not before been contemplated"); *Univ. of Ill. Found.* v. *Winegard Co.*, 402 F.2d 125, 127 (8th Cir. 1968) ("The statutory standard . . . is not 'predictability.' . . . Where logical exploration within known principles of the science achieves an unpredictable result, even though a commercially desirable one, the burden of nonobviousness is not necessarily overcome."); *Compton* v. *Metal Prods., Inc.*, 453 F.2d 38, 42 (4th Cir. 1971) ("'The ultimate question is whether a

hypothetical person having ordinary skill in the art would have readily found the same solution when addressing himself to the same problem.'").

Respondents have offered no response to this case law. And, although respondents try (at 2, 20) to divert attention from the on-point cases by citing *United States* v. *Adams*, 383 U.S. 39 (1966), that case is wholly inapposite given that the combination of elements at issue there was *not* obvious to try. See *id.* at 52 (certain "long-accepted factors, when taken together, would . . . deter any investigation into such a combination as is used by Adams").[2]

Astonishingly, Sanofi goes so far as to argue that *KSR* did not change the importance to the obviousness analysis of the "obvious to try" inquiry. BIO 27 ("*KSR* Did Not Reject the Principle that 'Obvious to Try' Is Generally Not the Standard for Obviousness."); contra 550 U.S. at 421-422 ("[T]he Court of Appeals . . . conclude[d], in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try.'"). Sanofi's agenda is to limit *KSR* so that it applies only to mechanical combinations and not to combinations of "reaction conditions and

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[2] Sanofi also cites *Sakraida* v. *Ag Pro, Inc.*, 425 U.S. 273 (1976), and *Anderson's-Black Rock, Inc.* v. *Pavement Salvage Co.*, 396 U.S. 57 (1969), but those cases stand only for the proposition that a combination of familiar elements that "yields no more than one would expect from such an arrangement" is not patentable. BIO 20 (quoting *KSR*, 550 U.S. at 417). We do not quarrel with that principle. Rather, as the cases cited at Pet. 14-15 show, the circumstances of *Sakraida* and *Anderson's-Black Rock* are not the *only* circumstances in which a patent is invalid for obviousness.

reagents" in chemistry and other "unpredictable arts," BIO 5, 22, 29; see also pages 10-11, *infra*, but surely *KSR* is not so provincial.

C. The reason "neither lower court made any . . . factual finding," BIO 3, that Sanofi's winning experiment was "obvious to try" is that they believed that the issue was irrelevant. Pet. 9; Pet. App. 27a, 112a. Thus, in arguing (at 2, 3, 21) that the experiment was in fact not "obvious to try," respondents assume answers to the very *KSR*-mandated inquiry that the courts below refused to conduct: Was there a design need or other pressure to solve a problem and a finite number of potential solutions such that Sanofi's chemists had good reasons to test the limited and well-known "variety of procedures" and "choices of reaction conditions and reagents," BIO 5, in an effort to single out the winning combination? See Pet. 13.

Sanofi (at 21) finds it significant that the result of any given choice of reaction conditions and reagents was not predictable, but *KSR*'s reference to a finite number of "predictable solutions" cannot mean that the exact outcome of an experiment or series of experiments must be perfectly knowable in advance. (After all, an experiment whose result is truly known in advance is a pointless experiment.) Instead, *KSR* was surely referring to scenarios in which any person having ordinary skill in the art predictably would test the same *limited set of choices*. And *KSR* requires not, as Sanofi suggests, an absolute "assurance," BIO 21, 22, that two enantiomers can be successfully isolated, but rather only a reasonable "anticipat[ion]," 550 U.S. at 421, that this is true.

Likewise, as regards salt formation, see Pet. 5 n.1, 6-7 n.2, it may be true that a person of skill in the art

would not have bet that the bisulfate form of the salt would turn out to be the most useful one. See BIO 10-11, 23. That is very different, however, from saying that the prior art deterred the investigation, see *Adams*, 383 U.S. at 52, that led to the bisulfate salt. So long as the person of ordinary skill had reasons to test a given set of acids that included sulfuric acid – and that point seems undisputed[3] – obviousness should not be defeated by the supposed unexpectedness of the identity of the winning substance, or of its properties.

Ultimately, respondents' analytical flaw is to assume that an inability to predict which one of a manageable number of known possibilities will work (even if it is reasonably likely that *one* of them will work) makes it not obvious to try the full set of possibilities. That is not the law.

II. The Federal Circuit Is Intractably Inconsistent

Respondents say that our "cynical assertion that case outcomes 'depend in large part on who the panelists are' . . . do[es] not withstand a methodical review." BIO 27-28. Unfortunately, it does. The 13 modern Federal Circuit cases discussed by petitioners and respondents in this connection (including this

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[3] See Pet. App. 73a (explaining that "the approach taken at Sanofi" to the identification of a suitable salt – namely, testing a large array of acids on the FDA-approved list, including many strong acids like sulfuric acid – was the same approach that a person of ordinary skill in the art would have used); see also *id.* at 74a ("[A] person of ordinary skill in the art would have known that . . . sulfuric acid [was one of] the three strongest acids used in pharmaceutical salts.").

case)[4] are divided almost evenly between decisions upholding and decisions invalidating patents on obviousness grounds. Yet, among those cases, there is not a single vote by any of the three panelists below to invalidate a patent for obviousness. On the contrary, in the relevant universe of cases, those three judges have each consistently voted to uphold (or to reverse a district court's or a panel's invalidation of) every one of the multiple patents they have been faced with.

Respondents contend that the Federal Circuit has "consistently held" that "unexpected and unpredictable results . . . are not automatically conclusive." BIO 24. In support of that assertion they cite *Pfizer* (as well as *Süd-Chemie*, 554 F.3d at 1009, which merely cites *Pfizer*). BIO 24-25. In *Pfizer*, however, two of the judges who decided this case wanted to rehear and reverse the panel decision because, on facts very similar to those at issue here, the *Pfizer* panel found obviousness using the "obvious-to-try" analysis endorsed by *KSR* and ignored by the panel

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[4] See BIO 24-25, 27-28 and Pet. 18-20 & n.6, 24 n.9 (citing *Pfizer, Inc.* v. *Apotex, Inc.*, 480 F.3d 1348, reh'g denied, 488 F.3d 1377 (2007); *Takeda Chem. Indus., Ltd.* v. *Alphapharm Pty., Ltd.*, 492 F.3d 1350 (2007); *Süd-Chemie, Inc.* v. *Multisorb Techs., Inc.*, 554 F.3d 1001 (2009); *Forest Labs., Inc.* v. *Ivax Pharms., Inc.*, 501 F.3d 1263 (2007); *Aventis Pharma Deutschland GmbH* v. *Lupin, Ltd.*, 499 F.3d 1293 (2007), reh'g denied (Dec. 3, 2007); *In re Kubin*, 561 F.3d 1351 (2009); *Muniauction, Inc.* v. *Thomson Corp.*, 532 F.3d 1318 (2008); *Bayer Schering Pharma AG* v. *Barr Labs., Inc.*, 575 F.3d 1341 (2009); *Abbott Labs.* v. *Sandoz, Inc.*, 544 F.3d 1341 (2008); *Ortho-McNeil Pharm., Inc.* v. *Mylan Labs., Inc.*, 520 F.3d 1358 (2008)); *Alza Corp.* v. *Mylan Labs., Inc.*, 464 F.3d 1286 (2006); *Procter & Gamble Co.* v. *Teva Pharms. USA, Inc.*, 566 F.3d 989 (2009)).

in this case. If this case and *Pfizer* had each been heard by the other's panel, each would have come out the other way. See Pet. 18-20.

These panel-dependent outcomes are possible only because some judges, like Sanofi (see BIO 22, 29), believe that *KSR*'s teachings on "obvious to try" apply differently or not at all in the so-called "unpredictable arts." We acknowledge that the Federal Circuit has sometimes gotten this issue right. It is impossible, however, to maintain seriously that there are not deep differences between Federal Circuit panels composed of different judges (and between the PTO and some Federal Circuit panels). Nor has the full Federal Circuit (which has had many opportunities to fix this situation) shown any inclination to reconcile its divergent cases. As we have explained, these inconsistencies create tremendous uncertainty in an area of the law where clarity and predictability are essential. See Pet. 20-21.

III. The Petition Raises A Public Policy Issue of Profound Importance

A. Respondents say that the '265 patent does not extend the monopoly on a patented compound already on the market. BIO 29. But that is exactly what it has done. The earlier '596 patent (whose validity is not disputed) claimed not just PCR4099 but its enantiomers and their salts. Pet. 5. It is undisputed that, even without the '265 patent, the earlier patent would have rewarded respondents with many profitable years of market exclusivity for Plavix. The only function of the '265 patent has been to extend Sanofi's monopoly by eight years, with no corresponding social benefit. See Pet. 16-17. As petitioners and their *amici* have explained, the economic and

medical consequences of gratuitously delaying generic competition in this fashion are gigantic. Br. of *Amici Curiae* AARP et al. 1-4, 10-13; Pet. 23, 24.

Sanofi attempts to justify this abuse by referring, mantra-like, to the "years of effort" and "tens of millions of dollars" it spent to develop the racemate. BIO 3-4, 7, 9, 23, 29-30. That is the same mistake that the Federal Circuit made, and it contributes to the necessity of further review. Pet. 21. As petitioners have pointed out (with no response from respondents), "sweat of the brow" is not and never has been the criterion for patentability. *Ibid.*

More fundamentally, the racemate and its enantiomers were already disclosed in (among other places) the prior-art '596 patent. See Pet. 6. The earlier investments were thus protected by the earlier patents. See Pet. 16, 21-22. Respondents seem to forget that the obviousness inquiry is whether "*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." 35 U.S.C. § 103 (emphasis added). See also *Graham* v. *John Deere Co.*, 383 U.S. 1, 17 (1966) ("Under § 103, the scope and content of the prior art are to be determined; *differences between the prior art and the claims at issue are to be ascertained*; and the level of ordinary skill in the pertinent art resolved." (emphasis added)). The validity of the '265 patent properly turns not on the size of Sanofi's investment in research and development since the 1970s, but on whether, *given that PCR4099 and its enantiomers were already disclosed*, one of the enantiomers *in*

isolation would have been obvious within the meaning of § 103.

Respondents also lose sight of the fact that the obviousness inquiry is an objective one. The actions of Sanofi's own chemists (including how much time they spent on which experiments), and Sanofi's subjective characterizations of the difficulty of each experiment are beside the point. Cf. *KSR*, 550 U.S. at 420 ("The question is not whether the combination was obvious to the patentee but whether the combination was obvious to a person with ordinary skill in the art."). Just as "[p]atentability shall not be *negatived* by the manner in which the invention was made," 35 U.S.C. § 103 (emphasis added), so too "the manner in which the invention was made" cannot possibly *confer* patentability.

B. Sanofi implies (at 28-30) that *KSR*'s lessons somehow carry less force in the life and chemical sciences because "unpredictability here is the rule, not the exception." It is critical, however, to remember *KSR*'s bottom-line message: "As progress beginning from higher levels of achievement is expected in the normal course, the results of ordinary innovation are not the subject of exclusive rights under the patent laws. Were it otherwise patents might stifle, rather than promote, the progress of useful arts." 550 U.S. at 427. See Pet. 15-17.

That message is no less applicable in the life and chemical sciences. Even in fields in which "unpredictability is the rule," there is such a thing as "ordinary innovation" and improvements that are "expected in the normal course." See Pet. 22-23. As the Federal Court of Australia recently explained in

ruling that the Australian counterpart of the '265 patent was obvious:

> Trial and error are normal, everyday parts of laboratory work and non-inventive laboratory experiments. That is what the hypothetical skilled worker in a laboratory does – *if the outcomes of experiments were known, there would be little point in doing them. That is the nature of everyday, non-inventive, research.*

Addendum, *infra*, 82 (emphasis added); see also *id.* at 19 ("Trial and error in the choice of salts involved non-inventive laboratory experiments."). The Australian court invalidated Sanofi's patent on clopidogrel bisulfate because it recognized what the Federal Circuit did not: Patents are not supposed to reward "normal, everyday" experimental work (the kind that yields "advances that would occur in the ordinary course," 550 U.S. at 419), even if aspects of that work are inherently unpredictable.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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