Supreme Court, U.S.
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No.

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

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Under the Patent Act, "a patent may not be obtained" if its subject matter is "obvious" when judged in light of the prior art. 35 U.S.C. § 103. In *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398 (2007), this Court addressed several "fundamental misunderstandings" in the Federal Circuit's long-standing approach to this nonobviousness requirement, including its mistaken view that "a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try.'" *Id.* at 421-422. In this case, the Federal Circuit, without even acknowledging that admonition, held that a chemical substance, once isolated, was nonobvious without any regard to "whether . . . it may have been 'obvious to try'" isolating the substance. App., *infra*, 27a. Its rationale was that certain properties of the isolated substance were not predictable. The question presented is:

> Whether, if an experiment was "obvious to try," a *prima facie* case of obviousness is automatically rebutted by a showing that the outcome of the experiment was not entirely predictable.

RULE 29.6 STATEMENT

The ultimate parent of petitioners Apotex, Inc. and Apotex Corp. is Sherfam Inc., which is not publicly traded. No publicly traded company owns 10% of the shares of petitioners or of any of their parent corporations.

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PETITION FOR A WRIT OF CERTIORARI

OPINIONS BELOW

The opinion of the Federal Circuit (App., *infra*, 1a-30a) is reported at 550 F.3d 1075. The district court's opinion (App., *infra*, 31a-124a) is reported at 492 F. Supp. 2d 353.

JURISDICTION

The judgment of the court of appeals was entered on December 12, 2008. App., *infra*, 1a. On March 26, 2009, the court of appeals denied a timely petition for panel rehearing and rehearing en banc. App., *infra*, 125a-126a. On May 29, 2009, the Chief Justice extended the time to petition for a writ of certiorari to and including July 24, 2009. This Court's jurisdiction is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

Section 103 of Title 35 of the United States Code provides, in pertinent part:

> (a) A patent may not be obtained . . . 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. Patentability shall not be negatived by the manner in which the invention was made.

STATEMENT

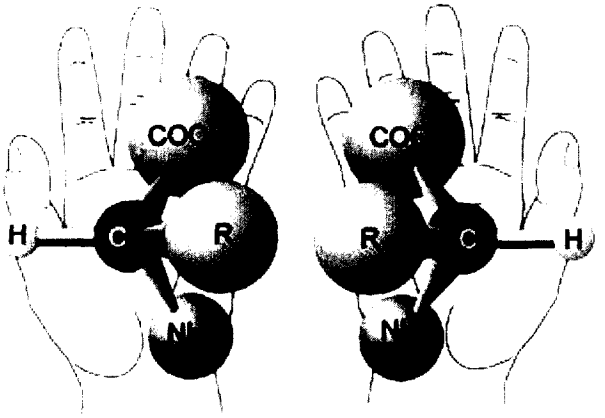
The question presented in this case arises

constantly in patent litigation. If an experiment is prompted by common knowledge in a field but its results cannot be predicted until the experiment is performed, does patentability turn on the *outcome* of the experiment, or is the inquiry rather whether the experiment was "obvious to try" in the first place? *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398 (2007), supplies a clear answer to this question, and yet the Federal Circuit addresses it in different ways depending on the particular three-judge panel that happens to hear a case. That confusion is entrenched; the Federal Circuit has repeatedly declined to review this issue en banc.

In this case, respondents (collectively "Sanofi") already had a patent on a substance that had shown promise as an anti-blood-clotting agent (*i.e.*, a blood thinner) and that was known to be a mixture of two closely related molecules. After obtaining that patent – which covered not just the mixture but each of the two constituent molecules – Sanofi isolated the two constituents, and found that one had especially pronounced anti-blood-clotting effects, whereas the other was inactive or toxic. Sanofi then obtained an additional patent that covered only the beneficial molecule in isolation. That molecule became the basis of the blockbuster blood-thinning drug Plavix. Plavix, however, was also protected by the first patent, which by itself gave Sanofi many highly profitable years of market exclusivity. The second patent's only function has been to prolong Sanofi's monopoly by eight years, and the question is whether the Federal Circuit correctly analyzed the validity of that patent.

A. Background Principles

Many organic molecules, including many drugs, exist in two forms that are exact mirror images. The two are alike in every way except for their spatial orientation: as with the left and right hand, the forms cannot be superimposed on each other. (This type of spatial asymmetry is known as "chirality." Many everyday objects, such as screws and airplane propellers, are chiral.) The two forms of such a molecule are called enantiomers, and can be described (depending on the direction in which they rotate polarized light) as either "left-handed" (or "levorotatory") or "right-handed" (or "dextro-rotatory"). *E.g.*, WILLIAM H. BROWN, ORGANIC CHEMISTRY 266-268, 278-279 (1995); App., *infra*, 8a. Here, for example, is a schematic illustration of the "handedness" of the enantiomers of a simple amino acid structure:



A substance consisting of an equal mixture of two enantiomers is called a "racemic" mixture, or a "racemate." *E.g.*, App., *infra*, 8a. The parties dispute whether, given a patent on a racemic mixture and its

constituent enantiomers, a later patent on only one of the enantiomers in isolation was obvious.

Enantiomers of the same molecule can have dramatically different biological effects. A notorious example is thalidomide, a tranquilizer that was marketed around the world from 1957 to 1961. *E.g.*, William A. Silverman, *The Schizophrenic Career of a "Monster Drug,"* 110 PEDIATRICS 404, 405-406 (2002). Thalidomide is a racemate, but it is believed that only the left-handed enantiomer is responsible for the sedative effects, whereas the right-handed twin produces birth defects. *E.g.*, John M. Brown & Stephen G. Davies, *Chemical Asymmetric Synthesis*, 342 NATURE 631, 631 (1989). Such "stereoselectivity" is common (if not usually so disastrous) in the world of organic chemistry and has been recognized by chemists for decades. See App., *infra*, 56a. "For racemic drugs, most often only one enantiomer exerts the beneficial effect, whereas the other enantiomer either has no effect, or exerts a detrimental effect. Thus, enantiomerically pure drugs should, more often than not, be more effective than their racemic counterparts." BROWN, *supra*, at 300.

For this reason, in February 1987 the U.S. Food and Drug Administration, following discussions with industry representatives, advised that sponsors of a new drug substance should "have either separated the various potential" enantiomers of the substance "or synthesized them independently." C.A. App. 17548. The agency also noted that individual enantiomers "may need to be studied for pharmacological and toxicological properties (and/or for safety and efficacy)." *Ibid.* Given these scientific and regulatory realities, "many drug companies have decided to

develop only single enantiomers of new chiral drugs." BROWN, *supra*, at 300.

B. The Patents Covering Plavix

Sanofi was no exception. On July 16, 1985, Sanofi was granted a patent on a substance known as PCR4099 and its chemical relatives, which were found to inhibit the aggregation of blood platelets. App., *infra*, 47a; Supp. App. S1, S3 col. 3 ll. 36-57; Supp. App. S12. The patent (U.S. Patent No. 4,529,596, or "the '596 patent") and its foreign counterparts (together, the "Aubert patents") acknowledged that PCR4099 and its relatives are chiral molecules that may exist in the form of two enantiomers, and claimed not only "both enantiomeric forms" of these compounds but also "their mixture." *E.g.*, Supp. App. S2 col. 1 ll. 38-41, S8 col. 13 ll. 17-18. The Aubert patents also claimed PCR4099's (and its enantiomers') "salts [formed from] pharmaceutically acceptable . . . acids." *Id.* at S8 col. 13 ll. 8-10; see also Supp. App. S23.[1]

Although the Aubert patents potentially covered a large number of chemical substances, it was clear that PCR4099 in particular merited further attention. The patents used it as their lead example of the class of molecules, and reported the results of

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[1] Drugs are commonly administered in the form of a "salt," which in chemical parlance refers to the product of a reaction between an acid and a base. Where, as here, the drug in question is a base, a pharmaceutical salt is formed by reacting it with an acid. See, *e.g.*, Note, *"Obvious to Try": A Proper Patentability Standard in the Pharmaceutical Arts?*, 76 FORDHAM L. REV. 2625, 2649 n.164 (2008) (citing WERMUTH & STAHL, INTRODUCTION TO HANDBOOK OF PHARMACEUTICAL SALTS: PROPERTIES, SELECTION, AND USE 1 (2002)).

tests in which PCR4099 exhibited very favorable anti-clotting activity. *E.g.*, Supp. App. S6-S7. In July of 1985, Sanofi promoted PCR4099 (but no other compound covered by the Aubert patents) in a paper and at a conference. App., *infra*, 54a. It was common knowledge, however, that drugs that appeared safe could exhibit serious side effects once on the market. *Id.* at 55a. And, as explained above, workers in the industry had strong reasons to try to separate chiral drugs into their enantiomers.

Accordingly, only a few months after obtaining the '596 patent, Sanofi's researchers in November 1985 asked a staff chemist to separate PCR4099 into its constituent enantiomers (which, as noted above, were covered by the Aubert patents). App., *infra*, 9a. He used a technique, known as "diastereomeric salt formation," that originated with Louis Pasteur in the 19th century. *Id.* at 10a. Testing revealed that the dextrorotatory ("right-handed") enantiomer was a highly effective anti-clotting agent whereas the levorotatory ("left-handed") twin had no such effects. At the same time, the left-handed enantiomer was far more toxic than the right-handed twin. *Ibid.* The right-handed enantiomer became known as "clopidogrel," and Sanofi applied for a separate U.S. patent on isolated clopidogrel plus its pharmaceutically acceptable salts. The patent issued on July 11, 1989, as No. 4,847,265 ("the '265 patent"). Supp. App. S29. Sanofi also determined that clopidogrel could be packaged and administered in the form of a bisulfate salt, known as clopidogrel bisulfate.[2] App.,

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[2] As explained in note 1 above, a salt is formed by reacting the drug with an acid. There is nothing particularly remarkable about this process, which is a "common practice in the

infra, 11a. Claim 3 of the '265 patent specifically recites this compound.

In 1997, the FDA approved the sale of clopidogrel bisulfate, which Sanofi exclusively markets as Plavix. App., *infra*, 32a. Plavix is routinely prescribed to treat or prevent heart attacks, strokes, and other cardiovascular events. The '596 patent expired in 2003, *id.* at 34a, but the '265 patent term lasts until 2011, *id.* at 33a.[3]

C. The District Court Proceedings

Petitioners (collectively "Apotex") manufacture and distribute generic drugs. In November 2001, Apotex applied under the Hatch-Waxman Act[4] for FDA approval to market clopidogrel bisulfate following the expiration of the '596 patent (whose validity is undisputed). Sanofi then sued for infringement of the '265 patent, see 35 U.S.C.

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pharmaceutical industry." Note, *"Obvious to Try"*, *supra* note 1, at 2649 n.164; see also *Pfizer, Inc.* v. *Apotex, Inc.*, 480 F.3d 1348, 1353 (Fed. Cir. 2007) ("Active drug molecules . . . are frequently made into pharmaceutically-acceptable acid addition salts to improve their bioavailability."). The FDA has approved a finite set of acids for this purpose. See, *e.g.*, App., *infra*, 73a. The bisulfate (also known as hydrogen sulfate) salt is obtained by reacting the drug with sulfuric acid, which is on the list of FDA-approved acids and was one of the first acids that Sanofi tested. *Id.* at 74a.

[3] That term is 20 years from the date of application (in this case February 12, 1988), see 35 U.S.C. § 154(c)(1), plus an extension to compensate for the FDA review period. See *id.* § 156.

[4] The Act (officially named the Drug Price Competition and Patent Term Restoration Act of 1984) governs the system of generic drugs. Among other things, the Act facilitates challenges to the validity of drug patents. See Pub. L. 98-417, 98 Stat. 1585 (1984).

§ 271(e)(2)(A), and Apotex counterclaimed for a declaration that the patent is invalid. App., *infra*, 3a. The district court held a bench trial, and ruled on June 19, 2007.

Confronting Apotex's obviousness challenge, Judge Stein observed that *Graham* v. *John Deere Co.*, 383 U.S. 1, 17-18 (1966), instructs a court to assess obviousness principally with reference to: (1) the scope and content of the prior art; (2) differences between the prior art and the claims at issue; and (3) the level of ordinary skill in the art. App., *infra*, 102a-103a. Judge Stein then assumed that Apotex had made out a *prima facie* case of obviousness given the prior disclosure of PCR4099 together with "the prior art teachings that (1) racemic compounds may be separated into their enantiomers; and (2) those enantiomers . . . may exhibit different biological activity or different degrees of the same type of biological activity exhibited by the racemate." *Id.* at 106a-107a.

The district court, however, believed that "it is not enough for Apotex to have shown that the [elements] found in Claim 3 of the '265 patent would have been 'obvious to try.'" App., *infra*, 103a. Relying on a series of Federal Circuit cases that antedated *KSR International Co.* v. *Teleflex Inc.*, 550 U.S. 398 (Apr. 30, 2007) – and without even citing *KSR* – the district court reasoned that "evidence of the fact that *any* property of clopidogrel bisulfate is unexpected as compared to PCR4099 or anything else in the prior art rebuts the presumption that clopidogrel bisulfate is obvious in view of its racemate." App., *infra*, 107a (emphasis added). That condition, the court added, was satisfied here because the precise properties of

the two enantiomers as compared with each other and the racemate could not have been "predict[ed] with a reasonable expectation of success." *Ibid.* The '265 patent accordingly was nonobvious, and this was true "[w]hether or not it may have been 'obvious to try' separating the enantiomers of PCR4099 and, secondarily, preparing its dextrorotary enantiomer as a bisulfate salt." *Id.* at 112a. The district court entered judgment in favor of Sanofi. *Id.* at 124a.

D. The Court of Appeals' Decision

The Federal Circuit affirmed. It agreed with the district court that clopidogrel bisulfate was nonobvious regardless of whether the compound was "obvious to try," see App., *infra*, 27a, endorsed the district court's focus on "the unpredictable and unusual properties of the dextrorotatory enantiomer," *id.* at 21a, and rejected Apotex's argument that "the correct inquiry is not whether the results obtained with the separated enantiomer were unexpected, but whether it would have been obvious to separate and test the enantiomers, based on the general knowledge that enantiomers can exhibit different properties," *id.* at 27a-28a.

The Federal Circuit highlighted testimony to the effect that "the therapeutic and toxic properties of the enantiomers" could not be predicted in advance, that "it was not predictable whether such differences, if any, would be weak, moderate, or strong, or how they would be manifested"; and that so-called "absolute stereoselectivity" (the two enantiomers of the same molecule having completely different biological effects) "is rare." App., *infra*, 23a. On this basis, the Federal Circuit upheld the district court's finding "that a person of ordinary skill in this field would not

reasonably have predicted that the dextrorotatory enantiomer [of PCR4099] would provide all of the [therapeutic] activity and none of the adverse neurotoxicity." *Id.* at 24a.

The Federal Circuit also reached beyond the reasons that the district court gave for holding the patent nonobvious (see App., *infra*, 104a-112a), pointing to the "difficulty" of the enantiomeric separation, and the time and effort needed to perform it. App., *infra*, 25a-26a. And the Federal Circuit agreed with the district court that "Sanofi's expenditure of tens of millions of dollars for several years of development of the racemate PCR4099, before [deciding to try] separating the enantiomers, also weighed against finding that separation would have been obvious," *id.* at 26a; App., *infra*, 108a.

The Federal Circuit also thought that rendering clopidogrel as the bisulfate salt was not obvious because the scientific literature listed many acids "as candidates for forming salts with basic drug compounds," and the parties' experts agreed that it was "unpredictable" whether any "particular acid-base combination" would yield a pharmaceutically suitable salt. App., *infra*, 27a. Finally, the Federal Circuit agreed with Sanofi that *KSR*'s lessons were inapplicable insofar as this case involved a procedure with an unpredictable result rather than a mechanical combination of familiar elements "having the properties of the known components." *Id.* at 29a-30a.

The Federal Circuit denied Apotex's petition for rehearing en banc. App., *infra*, 126a.

REASONS FOR GRANTING THE PETITION

The question presented arises constantly in many industries and has enormous economic importance. In many fields of science and other useful arts, experimenters using known methods frequently do not know how a particular substance or product will behave before they create it. Yet if, as the Federal Circuit's holding would have it, any new compound with at least some unpredictable properties is nonobvious, then nearly *every* new substance would qualify for a patent, and the patent system would "stifle, rather than promote, the progress of useful arts." *KSR Int'l Co.* v. *Teleflex Inc.*, 550 U.S. 398, 427 (2007).

KSR explained that a finding that an approach is "obvious to try" might well suffice to render the resulting invention obvious. The U.S. Patent and Trademark Office has followed suit. But the Federal Circuit has failed to apply that lesson consistently despite repeated unsuccessful requests for rehearing en banc and dissents by some of the court's members. This entrenched confusion harms brand-name product developers and would-be generic competitors; both types of companies make decisions about which products to develop and market based on standards of patentability.

Certworthiness of a Federal Circuit decision is often "found in the Federal Circuit's treatment of patentability standards, or in its treatment of an exceptionally significant patent, or in its application of Supreme Court precedent." EUGENE GRESSMAN ET AL., SUPREME COURT PRACTICE 287 (9th ed. 2007); see also *KSR*, 550 U.S. at 407 ("Because the Court of Appeals addressed the question of obviousness in a

manner contrary to § 103 and our precedents, we granted certiorari."). This case presents every one of those circumstances, and more. This Court should grant review, resolve the confusion in the Federal Circuit's case law, and clarify that *KSR* applies even when certain aspects of the art are inherently unpredictable.

I. The Court of Appeals Has Failed To Heed This Court's Admonition That "Obvious To Try" *Can* Render an Invention Obvious

A. *KSR* explicitly rejected the analysis used below. In *KSR*, the Federal Circuit had deployed a series of doctrines to avoid concluding that a patent was obvious, even though the invention – titled "Adjustable Pedal Assembly With Electronic Throttle Control" – was just a mechanical combination of two already well-known components. See 550 U.S. at 406, 413-415. The Federal Circuit thought it irrelevant "[t]hat it might have been obvious to try the combination of [an adjustable pedal assembly] and [an electronic] sensor," because, according to the Federal Circuit, "'obvious to try' has long been held not to constitute obviousness." *Id.* at 414 (internal quotation marks omitted).

This Court disagreed:

> [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." When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill

> has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.

550 U.S. at 421 (citation omitted).

The district court and the Federal Circuit flatly ignored this teaching. (The district court ruling did not even cite *KSR*, which antedated the ruling by two months.) See App., *infra*, 103a (quoting Federal Circuit: "We have consistently held that 'obvious to try' is not to be equated with obviousness under 35 U.S.C. § 103."); App., *infra*, 27a (agreeing that the '265 patent was nonobvious "[w]hether or not it may have been 'obvious to try' preparing clopidogrel bisulfate"). Apotex, however, was entitled to have the courts below ask the questions posed by this Court in *KSR*: whether there was a "design need" or other "pressure" to solve a problem (namely, the isolation of the enantiomers of a promising racemate and the preparation of a pharmaceutically acceptable salt) and a "finite number of identified, predictable solutions" (namely, the reagents and concentrations that one varies in order to separate enantiomers and prepare a pharmaceutical salt) such that Sanofi's workers had good reason "to pursue the known options within [their] technical grasp." Had the courts below asked those crucial questions mandated by *KSR*, they might have recognized that Sanofi's successful enantiomeric separation and salt formation was "the product not of innovation but of ordinary skill and common sense."

B. Instead, the courts below focused on the *outcome* of Sanofi's experiments, and in particular on whether any aspect of that outcome was unexpected. See App., *infra*, 107a ("[E]vidence of the fact that *any* property of clopidogrel bisulfate is unexpected . . . rebuts the presumption that clopidogrel bisulfate is obvious in view of its racemate." (emphasis added)). Yet both sides agree that it was known that the properties (both therapeutic and toxic) of enantiomers often differ, even if the exact nature and degree of difference could not have been known. And it is undisputed that the properties of a racemate are the sum of the properties of its enantiomers. Thus, given a known racemate, the only unknown will be the precise *allocation* of its properties to the enantiomers.[5] In hanging patentability on this "known unknown," the Federal Circuit essentially said that any element of unpredictability or unexpectedness in an experiment suffices to patent the result.

That fixation on unexpectedness or unpredictability has no support in, and in fact clashes with, this Court's decisions. When "the prior art discloses the method of making an article having the characteristics of the patented product," this Court has noted, the patent is invalid, "[even] though all the advantageous properties of the product had not been fully appreciated." *Gen. Elec. Co.* v. *Jewel Incandescent Lamp Co.*, 326 U.S. 242, 248 (1945). In fact, by the end of the 19th century, "nothing [wa]s better settled in this [C]ourt than that the application of an old process to a new and analogous purpose does not

[5] The testing required to determine those properties once the enantiomers are isolated is routine (if time-consuming), and nobody has suggested otherwise.

involve invention, *even if the new result had not before been contemplated.*" *Ansonia Brass & Copper Co.* v. *Elec. Supply Co.*, 144 U.S. 11, 18 (1892) (emphasis added).

This point was appreciated by at least some of the courts of appeals before the Federal Circuit was created. See *Univ. of Ill. Found.* v. *Winegard Co.*, 402 F.2d 125, 127 (8th Cir.) ("The statutory standard of patentability under § 103 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."), cert. denied, 394 U.S. 917 (1969); *Compton* v. *Metal Prods., Inc.*, 453 F.2d 38, 42 (4th Cir.) ("'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.'"), cert. denied, 406 U.S. 968 (1972). Having been rebuffed in *KSR* for according too little weight to the fact that a new approach was "obvious to try," the Federal Circuit has resurrected long-discarded notions to try to rebut the inference that arises from the obviousness of trying a particular approach.

What is more, the Federal Circuit's approach is fundamentally inconsistent with one of *KSR*'s core animating principles: "Granting patent protection to advances that would occur in the ordinary course without real innovation retards progress." 550 U.S. at 419. The whole reason for the nonobviousness requirement is that the patent system is supposed to reward not (as the decisions below seem to have assumed) every single incremental advance, but rather *only advances that would have been less likely*

without the promise of a patent. The "carefully crafted bargain" embodied in the patent system confers exclusive rights for a period of years only as a means to "the ultimate goal" of "bring[ing] new designs and technologies *into the public domain.*" *Bonito Boats, Inc.* v. *Thunder Craft Boats, Inc.*, 489 U.S. 141, 150-151 (1989) (emphasis added); accord *Pfaff* v. *Wells Elecs., Inc.*, 525 U.S. 55, 63-64 (1998). If an invention was going to enter the public domain anyway, then almost by definition a separate patent on it only "retards progress."

The right-handed enantiomer of PCR4099 turned out to be a better drug than the racemic mixture, but there are excellent reasons to believe that Sanofi would have separated PCR4099 into its components (and then selected an appropriate salt) "in the ordinary course." (Those reasons include PCR4099's known properties as a blood thinner, and the potential benefits of separating a racemic mixture into its constituent enantiomers.) And if no additional inducement was needed for this incremental advance, then additional exclusivity cannot possibly promote the purposes of the patent system.

In fact, it is telling that Sanofi would have been rewarded handsomely for its investments even without the later '265 patent. The earlier '596 patent gave Sanofi 20 years of exclusive rights in the United States to PCR4099 and its component enantiomers. That period expired only after Plavix had been on the market for five or six years as one of the world's top-selling drugs – and could have lasted even longer if Sanofi had relied only on the '596 patent to protect Plavix. See note 3, *supra*. Conferring an additional eight years of exclusivity through the '265 patent, see

page 7 *supra*, is an abuse of the patent system's "carefully crafted bargain" – it has postponed competition in the market for an important drug with no corresponding societal benefit.

In sum, the Federal Circuit was quite wrong to distinguish *KSR* on the ground that it involved a mechanistic combination of known components rather than a chemical refinement with a not-fully-predictable result. The basic lesson of *KSR* is that not every incremental advance should qualify for twenty years of exclusivity. That lesson is not limited to mechanical engineering, nor is it any less applicable simply because some aspects of a technology are inherently unpredictable.

C. The approach adopted below runs counter to that of the PTO and contributes to incoherence in the Federal Circuit's case law. Following *KSR*, the PTO issued new examination guidelines for determining obviousness. The guidelines, which cite and closely track *KSR*, are wholly inconsistent with the analysis employed by the courts below. They direct a patent examiner to reject claims as "Obvious To Try" if he or she finds:

> (1) . . . that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
>
> (2) . . . that there had been a finite number of identified, predictable solutions to the recognized need or problem;
>
> (3) . . . that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and

> (4) whatever additional findings based on the *Graham* factual inquiries [(see page 8, *supra*)] may be necessary . . . to explain a conclusion of obviousness.

PTO, *Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of [KSR]*, 72 FED. REG. 57526, 57529, 57532 (2007).

As "Example 1" of this analysis, the guidelines discuss *Pfizer, Inc.* v. *Apotex, Inc.*, 480 F.3d 1348 (Fed. Cir.), cert. denied, 128 S. Ct. 110 (2007). In that case, the patentee had argued that the results of forming a particular pharmaceutical salt "would have been unpredictable, and therefore were nonobvious." 75 FED. REG. at 57532. The panel, however, "*rejected the notion that unpredictability could be equated with nonobviousness* here, because there were only a finite number (53) of pharmaceutically acceptable salts to be tested." *Ibid.* (emphasis added). In other words, a degree of unpredictability does not overcome "obvious to try."[6]

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[6] Similarly, the PTO uses as "Example 2" of "Obvious To Try" another Federal Circuit case in which, according to the PTO, "it would have been obvious to try the known methods . . . , with a reasonable expectation of success. The court was not swayed by arguments of a lack of absolute predictability." *Ibid.* (citing *Alza Corp.* v. *Mylan Labs., Inc.*, 464 F.3d 1286 (2006)). Both *Pfizer* and *Alza* were decided between the *KSR* cert. grant and opinion, at a time when Federal Circuit judges had made no secret of their apprehension of a potential reversal in *KSR*. See 550 U.S. at 421 ("We note the [Federal Circuit] has since elaborated a broader conception of [its obviousness] test than was applied in the instant matter." (citing *Alza*)). The PTO's third and final example of "Obvious to Try" was *Ex Parte Kubin*, a PTO administrative appeal since affirmed by the Federal Circuit. The *Kubin* decisions closely track *KSR*'s discussion of "obvious

As if to provide a neat demonstration of the inconsistency in the Federal Circuit's obviousness jurisprudence, in the present case, three different Federal Circuit judges reached the opposite conclusion from the *Pfizer* panel about the obviousness of the salt formation, even though Sanofi had merely chosen from among *the exact same list of 53 acids* at issue in *Pfizer*. See, *e.g.*, App., *infra*, 70a, 73a; see also note 2, *supra*. The difference between the two cases is explained not by their facts (which as regards salt formation were quite similar), but by the legal analysis. The panel in this case relied on what the *Pfizer* panel and the PTO have disclaimed: the unpredictability of the chemical reactions. What is more, three of the Federal Circuit's judges wanted the court to rehear *Pfizer* en banc. They criticized *Pfizer*'s use of an "obvious to try" analysis (even though by then *KSR* had endorsed it) and emphasized the supposedly "unexpected properties" of the patented substance. See 488 F.3d 1377, 1379-1384 (2007). Two of those dissenting three judges were panelists in this case.

Those judges' views have tended to prevail in other cases as well. For example, the author of the opinion below decided in another recent case that a patented drug delivery formulation was likely not "obvious to try" under *KSR*, even though it was within a finite universe of known options suggested

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to try," see 72 FED. REG. at 57532; *In re Kubin*, 561 F.3d 1351, 1358-1361 (Fed. Cir. 2009), but *Kubin* does not present the question whether a showing of any unpredictability negates obviousness based on "obvious to try." See 561 F.3d at 1360 ("[T]his record shows that one of skill in this advanced art would find these claimed 'results' profoundly 'predictable.'").

by the prior art, because "the results obtainable from" any one "selected component" were not predictable. *Abbott Labs.* v. *Sandoz, Inc.*, 544 F.3d 1341, 1350-1351 (Fed. Cir.), reh'g denied (Feb. 23, 2009).[7] And a panel led by another of the judges who decided the present case approved a district court's pre-*KSR* dictum to the effect that "unexpected results" could rebut a *prima facie* case of obviousness. See *Takeda Chem. Indus., Ltd.* v. *Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1354, 1359, 1360-1362 (Fed. Cir.), reh'g denied (Sept. 27, 2007), cert. denied, 128 S. Ct. 1739 (2008).

Thus while at least one Federal Circuit panel (and the PTO) have focused correctly on the obviousness of the path followed to reach a result, most of the others have focused on whether the properties of the result could have been precisely predicted in advance, implicitly assuming that *KSR* does not apply when there is such unpredictability. The approach seems to depend in large part on who the panelists are. And yet the Federal Circuit (in stark contrast to the PTO) is making no effort to harmonize its rulings with each other and with *KSR*.

The result is enormous uncertainty in an area of the law in which certainty is crucial. Companies make research, development, investment, and marketing decisions based on predictions about whether potential inventions will qualify for patents in the PTO, and whether issued patents will survive court

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[7] This rationale was advanced by Judge Newman's "Opinion for the court," *id.* at 1343. One judge dissented. See *id.* at 1378. The third concurred in the judgment, but without joining this section of the opinion or authoring another.

challenges. When the Federal Circuit's behavior is not only inconsistent but regularly in conflict with that of the PTO, it becomes impossible to make reliable predictions. This kind of uncertainty is extraordinarily harmful to consumers as well as companies. For example, in the pharmaceutical industry, such uncertainty emboldens brand companies to seek to enforce questionable patents and deters potential competitors from challenging those efforts.

D. The Federal Circuit's subsidiary justifications for upholding the patent – namely that Sanofi had spent tens of millions of dollars on developing the racemate *before* deciding to separate the enantiomers, and that separating the enantiomers was time- and labor-intensive, see page 10, *supra* – are also misplaced and will work great mischief if left in place. First of all, "sweat of the brow" is not a criterion for patentability. See 35 U.S.C. § 103(a) ("Patentability shall not be negatived by the manner in which the invention was made."); *Compton*, 453 F.2d at 42 ("Neither is the amount of time spent by Compton in devising the method a controlling factor."); cf. *Feist Publ'ns, Inc.* v. *Rural Tel. Serv. Co.*, 499 U.S. 340, 359-360 (1991). Were it otherwise, many laborious but unimaginative undertakings that would "occur in the ordinary course" and do not represent "real innovation," 550 U.S. at 419, would qualify for a patent.

What is more, the investment that impressed the lower courts mostly took place *before* the Aubert patents and Sanofi's public promotion of PCR4099 – the very prior art disclosures against which the later patent must be judged. Sanofi's investment, in other words, was protected by – and rewarded with – the

earlier patents. To reward Sanofi for its *earlier* investment by upholding a *later* patent on an inexorable minor advance is to violate the patent bargain in precisely the way that *KSR* warned against.[8]

II. The Question Presented Arises Constantly and Is Tremendously Important

The patent statute covers (among several other categories of invention) "new and useful . . . composition[s] of matter." 35 U.S.C. § 101. But it is rarely if ever possible to know all of the properties of a new composition of matter before it is created. See, *e.g.*, CHISUM ON PATENTS § 5.04[6], at 5-472 (2008) ("Because of the unpredictable nature of chemical reactions, a newly-synthesized compound may be very similar in structure to known and existing compounds and yet exhibit very different properties."). In fields devoted to generating new compositions of matter, workers of ordinary skill conduct experiments every day in the belief that they are reasonably likely to obtain a useful result – even though they cannot

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[8] Contrary to what the Federal Circuit apparently assumed, it is not at all clear that a patent should be available as the end product of any successful research and development work. An influential academic account offers the insight that a patent is designed to claim a space in which, for a limited time, the patentee alone has the right to "prospect" by developing "known technological possibilit[ies]" within that space. Edmund W. Kitch, *The Nature and Function of the Patent System*, 20 J. L. & ECON. 265, 266 (1977). A patent, in other words, can be seen as an initial condition for, not the culmination of, a research and development effort. The '596 patent appropriately ensured that only Sanofi could work with PCR4099, but that does not mean that all of the additional work Sanofi did with PCR4099 in turn should qualify for a new patent.

perfectly predict what the result will be. If any degree of unpredictability or unexpectedness sufficed to impart patentability, then virtually every new substance could be removed from the public domain for at least 20 years, even when creating or isolating it was the obvious thing to do.

Accordingly, the question presented – which the leading treatise describes as a "key problem" in patent law, CHISUM, *supra*, § 5.04[6], at 5-472 – is critical to the public's ability to access the fruits of fields like pharmacology, biotechnology, industrial and agricultural chemistry, and the like. See, *e.g.*, *Pfizer*, 480 F.3d at 1367 (recognizing potential impact on the pharmaceutical industry of an obviousness standard based on "obvious to try"); Jonathan J. Darrow, *The Patentability of Enantiomers: Implications for the Pharmaceutical Industry*, 2007 STAN. TECH. L. REV. 2, 3 & n.20 (2007) (noting significance to chemical industries generally of patentability of chiral molecules); Note, *Putting the Brakes on Drugs: The Impact of KSR v. Teleflex on Pharmaceutical Patenting Strategies*, 42 GA. L. REV. 905 (2008); Note, *"Obvious To Try": A Proper Patentability Standard in the Pharmaceutical Arts?*, 76 FORDHAM L. REV. 2625 (2008). The decision below, and others like it, create an incentive to game the system by engaging in what might be called the inventing of patents rather than the patenting of inventions. And when, as in this case and many others, the product with the supposedly "unpredicted" features is in a category to which one already has exclusive rights, the only effect of the additional patent is gratuitously to extend a monopoly that was supposed to be of limited duration.

This phenomenon is of particular concern in the pharmaceutical industry, because it allows companies with patents on brand-name drugs to delay consumers' access to generic drugs, which not only are themselves cheaper but also provide competition that often reduces the prices of brand-name drugs. Limiting competition in turn has adverse effects on the overall cost and availability of heath care. There will always be new methods of modifying drugs or isolating promising variants, and it will never be possible to predict all of the properties of a new substance. The Federal Circuit's decision, by providing a roadmap for pharmaceutical patent-holders seeking to extend monopolies that no longer serve any social purpose, contributes to the needless escalation of already soaring health-care costs.

Cases presenting this issue abound. In the past three years alone, the Federal Circuit has issued published – but inconsistent – decisions in at least seven such cases.[9] Moreover, the specific fact pattern presented here (an enantiomer patented over the racemic mixture) is a good vehicle for examining the issue. For one thing, it neatly illustrates the question presented. In fact, this is the paradigmatic (though far from only) context in which the question presented arises. See Darrow, *The Patentability of Enantiomers*, *supra*, at 37-51. And the pertinent scientific principles here are limited in number and

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[9] In addition to this case, see *Abbott Labs.*, *supra*; *Takeda Chem.*, *supra*; *Pfizer*, *supra*; *Alza*, *supra*; *Aventis Pharma Deutschland GmbH* v. *Lupin, Ltd.*, 499 F.3d 1293, 1301-1303 (Fed. Cir. 2007), reh'g denied (Dec. 3, 2007); *Procter & Gamble Co.* v. *Teva Pharms. USA, Inc.*, 566 F.3d 989, 994-998 (Fed. Cir. 2009).

relatively accessible, especially in comparison to other pharmacology and biotechnology cases.

Finally, litigation over this fact pattern has become quite common, giving this Court the benefit (especially valuable in a technical area) of reference points from other courts' reactions to similar cases. See, *e.g.*, *Aventis Pharma Deutschland GmbH* v. *Lupin, Ltd.*, 499 F.3d 1293 (Fed. Cir. 2007); *Forest Labs., Inc.* v. *Ivax Pharms., Inc.*, 501 F.3d 1263 (Fed. Cir. 2007); *Pfizer Inc.* v. *Ranbaxy Labs. Ltd.*, 405 F. Supp. 2d 495, 516-519 (D. Del. 2005); *Ortho-McNeil Pharm., Inc.* v. *Mylan Labs., Inc.*, 348 F. Supp. 2d 713, 749-755 (N.D.W. Va. 2004); *Emory Univ.* v. *Glaxo Wellcome Inc.*, 44 U.S.P.Q.2d 1407, 1414 (N.D. Ga. 1997).

In sum, this Court should review an approach to patentability that will "stifle, rather than promote, the progress of useful arts," *KSR*, 550 U.S. at 427. Because the Federal Circuit has shown no interest in resolving the confusion in its cases, the perception of an appellate lottery on the question presented will endure until this Court speaks. This Court should clarify that *KSR*'s guidance is not limited to cases involving mechanical combinations, but applies even when there is an element of unpredictability to the technology. This is the right case in which to do so.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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