No. 18-_____

In the Supreme Court of the United States

ACCORD HEALTHCARE, INC. and
INTAS PHARMACEUTICALS LTD.,

Petitioners,

–v–

UCB, INC.; UCB BIOPHARMA SPRL;
RESEARCH CORPORATION TECHNOLOGIES, INC.;
and HARRIS FRC CORPORATION,

Respondents.

On Petition for Writ of Certiorari to the
United States Court of Appeals for the Federal Circuit

PETITION FOR WRIT OF CERTIORARI

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QUESTION PRESENTED

Did the Federal Circuit commit error in holding that a patent claim to an obvious modification of a prior art compound was not invalid as obvious under 35 U.S.C. § 103(a) because the prior art compound would not have been selected as a "lead compound" that was "most promising to modify in order to improve upon its activity and obtain a compound with better activity?

PARTIES TO THE PROCEEDING

Petitioners and Defendant-Appellants Below

- Accord Healthcare, Inc.
- Intas Pharmaceuticals Ltd., the parent company of Accord Healthcare, Inc.

Respondents and Plaintiffs-Appellees Below

- UCB, Inc.
- UCB Biopharma Sprl
- Research Corporation Technologies, Inc.
- Harris FRC Corporation

Respondents and Defendants-Appellants Below

Fed. Cir. Dkt. 2016-2610; 2016-2710

- Alembic Pharmaceuticals Ltd.
- Alembic Pharma Limited
- Actavis, Inc. nka Allergan Finance, LLC

Fed. Cir. Dkt. 2016-2610; 2016-2698

- Amneal Pharmaceuticals LLC
- Amneal Pharmaceuticals of New York, LLC

Fed. Cir. Dkt. 2017-1001

- Apotex Corp
- Apotex, Inc.

Fed. Cir. Dkt. 2016-2610; 2016-2698

- Aurobindo Pharma Ltd.
- Aurobindo Pharma USA, Inc.

Fed. Cir. Dkt. 2016-2610; 2016-2698

- Breckenridge Pharmaceutical, Inc.

Fed.Cir. Dkt. 2016-2610; 2016-2683

- Mylan Pharmaceuticals, Inc.
- Mylan, Inc.

Fed. Cir. Dkt. 2016-2610; 2016-2698

- MSN Laboratories Pvt. Ltd.

Fed. Cir. Dkt. 2016-2610; 2016-2698

- Sun Pharma Global FZE
- Sun Pharmaceutical Industries, Ltd.

Fed. Cir. Dkt. 2016-2610; 2016-2698

- Watson Laboratories, Inc. Florida, nka Actavis Laboratories, FL, Inc.
- Watson Pharma, Inc. nka Actavis Pharma, Inc.

Fed. Cir. Dkt.2016-2610; 2016-2685

- Zydus Pharmaceuticals (USA) Inc.
- Cadila Healthcare Limited

CORPORATE DISCLOSURE STATEMENT

Accord Healthcare, Inc. is a 100% owned subsidiary of Intas Pharmaceuticals, Limited. No publicly held corporation owns more than 10% of the stock of Intas Pharmaceuticals, Ltd.

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JURISDICTION

The opinion of the Court of Appeals was entered on May 23, 2018. (Pet.App.1a-43a). Petitions for rehearing *en banc* were filed and an order denying rehearing was entered on August 24, 2018. (Pet.App.160a-162a). This Court's jurisdiction is invoked under 28 U.S.C. § 1254(1). The district court had jurisdiction to hear plaintiffs' claim for alleged patent infringement under 28 U.S.C. § 1338(a). The Federal Circuit had jurisdiction to hear Defendants' appeal under 28 U.S.C. § 1295(a)(1).

STATUTORY PROVISION INVOLVED

This case concerns the standard of patentability set forth in the Patent Act, 35 U.S.C. § 103(a), which provides:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102, 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 OF THE CASE

This case presents a recurring issue of significance to every pharmaceutical compound patent and to the consistent application of patent law. Following this Court's decision in *KSR Int'l v. Teleflex, Inc.*, 550 U.S. 398 (2007), the Federal Circuit applied a new obviousness standard unique to chemical compound patents that is plainly at odds with this Court's standard for obviousness, at odds with the plain terms of 35 U.S.C. § 103(a), and in direct conflict with Federal Circuit's own earlier *en banc* ruling in *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990) as well as other Federal Circuit precedent.

This Federal Circuit obviousness standard, commonly referred to as the "lead compound" analysis, holds that a patent claim to a pharmaceutical compound cannot be found to be obvious based on its close relation to or explicitly taught modification of a prior art compound unless the prior art compound would have been selected as a lead compound by a person of ordinary skill. The Federal Circuit further defines a "lead compound" as "a compound in the prior art that would be most promising to modify in order to improve

upon its activity and obtain a compound with better activity." The Federal Circuit in this case described the rule it now applies to determine obviousness of compounds:

> We have held that to demonstrate that a new chemical compound would have been prima facie obvious over a particular prior art compound based on a lead compound analysis, the court follows a two-part inquiry. First, "the court determines whether a chemist of ordinary skill would have selected the asserted prior art compounds as lead compounds, or starting points, for further development efforts." Second, the court determines "whether the prior art would have supplied one of ordinary skill in the art with a reason or motivation to modify a lead compound to make the claimed compound with a reasonable expectation of success." A lead compound is "a compound in the prior art that would be most promising to modify in order to improve upon its . . . activity and obtain a compound with better activity." (emphasis added). (citing *Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1291 (Fed. Cir. 2012) and *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007)). 890 F.3d at 1328.

(Pet.App.26a-27a).

Under this lead compound standard of obviousness, a prior art compound is not compared to the claimed compound to determine whether any differences between the prior art compound and the patent claim

are obvious unless the prior art compound is given the status of a lead compound. Accordingly, an obvious variant of a prior art compound becomes patentable if the prior art compound is not found to be a "lead compound".

This patent infringement action plainly demonstrates why the lead compound analysis as now applied by the Federal Circuit is at odds with the controlling obviousness standards.

Respondents UCB, Inc. et. al. brought a patent infringement suit against petitioner Accord Healthcare, Inc. *et. al.* and other defendants asserting infringement of U.S. Patent RE 38,551 (the " '551 patent") arising from the defendants' filing of Abbreviated New Drug Applications with the FDA to market the anticonvulsant compound lacosamide sold by UCB, Inc. under the brand name "Vimpat®". The '551 patent claims the R-stereoisomer[1] of a prior art compound known as "107e" and its use as an anticonvulsant drug. (The R-stereoisomer of 107e is now named "lacosamide").

There were three asserted claims in the '551 patent in suit. Claim 9 was to a prior art compound known

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[1] Stereoisomers, also called enantiomers in this context, of chemical compounds have identical chemical structures but are mirror images of each other [Appx.700]. A physical composition that is a 50/50 mixture of two stereoisomer molecules is called a 'racemate' or 'racemic mixture.'" [201 F.Supp.3d at 501] (Pet.App.56a). For this class of compounds, the R-stereoisomer is sometimes referred to in the prior art references as the D-enantiomer or D-stereoisomer and the S-stereoisomer as the L-enantiomer or L-stereoisomer. For clarity, this petition will use the terms R-stereoisomer and S-stereoisomer when describing references to the stereoisomers. [Appx.701-703].

as 107e (described in chemical terminology), where at least 90% of the molecules were in the form of the R-stereoisomer of that compound. (Pet.App.12a). Claim 10 was to a pharmaceutical composition of the compound of claim 9 (Pet.App.12a), and claim 13 was to a method of treatment of nervous system disorders with an anticonvulsant amount of the compound of claim 9. (Pet.App.13a).

A prior art thesis by LeGall [Appx.4882-5073] disclosed the structural formula of compound 107e as a member of a class of anticonvulsant compounds known as Functional Amino Acids ("FAA compounds") [Appx.5028-5029; 5050][2], and stated that compound 107e "may have good anticonvulsant activity" due to its close structural relation to another FAA compound with such activity. [Appx.5050] (Pet.App.42a). In addition to the LeGall Thesis, the plaintiff's prior art patent 5,378,729 (the "'729 patent") [Appx.4767-4806] also taught that compound 107e was an effective anticonvulsant treatment. The '729 patent disclosed and claimed a chemical formula describing effective anticonvulsant compounds useful in treating nervous system disorders such as epilepsy. Compound 107e was a specific embodiment of that claimed formula of effective anticonvulsants. [Appx.734-735]

It was undisputed that any person of ordinary skill in the art would have known that the formula of compound 107e represents two distinct stereoisomer molecules—an R and an S. [Appx.718-723; 1416-1418] The LeGall Thesis further disclosed that the R-stereoisomer was 13 times more potent than the S-stereo-

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2 "Appx" citations are to the Appendix in the Federal Circuit.

isomer in closely related FAA compounds. [Appx. 4937] Several prior art articles reported that the R-stereoisomer of related FAA compounds had all, or nearly all, of the anticonvulsant activity. [Appx.3235; 3724] (Pet.App.122a-123a). The prior art '729 patent expressly taught that the R-stereoisomer was preferred. [Appx.4773] (Pet.App.123a).

It was undisputed that making a preparation solely of R-stereoisomer of compound 107e was enabled. [Appx.1418]

The only difference between the prior art disclosure of compound 107e and the compound of claim 9 of the '551 patent is that compound 107e was presented in the prior art as a structural formula representing both the R-stereoisomer and S-stereoisomer, and was made by LeGall in that 50%-R and 50%-S mixed form; whereas the claim of the '551 patent requires that at least 90% of the compound 107e molecules be in the R-stereoisomer form. In addressing obviousness double-patenting, the district court found that this difference was an obvious one holding:

> [A] POSA [person of ordinary skill in the art] would have found it obvious to isolate the R-enantiomer of any FAA that was selected for further development. Plaintiffs did not offer any evidence or data that would support a contrary conclusion. 201 F.Supp.3d. at 531.

(Pet. App.123a).

That finding—*i.e.* the only difference between the prior art compound 107e and the patent claim of the isolated R-stereoisomer of compound 107e is an obvious difference—mandated a finding of obviousness of the

compound claim in the '551 patent. That necessary conclusion was avoided by the lead compound analysis with the irrelevant and subjective finding that a person of ordinary skill would have selected something other than compound 107e for further development.

Anyone simply reading these few prior art references would have literally been taught exactly what the '551 patent claimed—the R-stereoisomer of 107e is an effective anticonvulsant compound. Compound 107e was described in the art as an FAA anticonvulsant compound and it was known that the R-stereoisomer of such compounds contained virtually all the anticonvulsant activity. The '551 patent claims are simply a restatement of what literally appears in the prior art and they should have been found obvious.

The lead compound theory replaces this Court's objective standard comparing the scope and content of the prior art to the patent claim with a subjective test to determine which prior art compound the person of skill would select as most promising. Its focus is not, as it should be, on the objective test of what a person of ordinary skill in the art would have known, but rather on a subjective judgment of what a hypothetical person of ordinary skill would have chosen to do with prior art knowledge.

The Federal Circuit has repeatedly failed to reconcile its lead compound analysis with this Court's, and the Federal Circuit's own precedents, including *en banc* precedent, and in fact, it cannot be reconciled. The facts of this case present this important question in the plainest possible terms.

A. Proceedings Below

A trial to the court was held in the District of Delaware between November 9 and 13, 2016. The defendants raised three grounds of invalidity: anticipation of the compound claim, obviousness of all claims[3], and double patenting for all asserted claims. The district court rejected all three defenses.

The Federal Circuit, in a 2 to 1, opinion affirmed the district court.

A petition for rehearing *en banc* was filed by Accord Healthcare, Inc. and Intas Pharmaceuticals, Ltd., and was denied by the Federal Circuit on August 24, 2018. Other defendants also filed a separate petition for rehearing *en banc* and that petition was also denied on the same date.

REASONS FOR GRANTING REVIEW

I. THE FEDERAL CIRCUIT "LEAD COMPOUND" ANALYSIS CONFLICTS WITH THIS COURT'S OBVIOUSNESS STANDARD

The lead compound analysis undermines the standard of obviousness set forth by this Court in *KSR Int'l v. Teleflex, Inc.*, 550 U.S. 398, 406 (2007), and disregards the very notion of invention—that is, an inven-

[3] An alternate theory of obviousness was that it was obvious to "purify" compound 107e by making the R-stereoisomer only, and that the lead compound theory did not apply to a purification even if that standard was otherwise appropriate. That defense was also rejected.

tion must at least be a new idea that adds to what is already known in the art, and not merely a selection of something previously known.

The Federal Circuit lead compound analysis, as applied in this case, permits the patenting of pharmaceutical compounds and their use that were fully taught or suggested by the prior art unless, in addition, it is proven by clear and convincing evidence that a person of ordinary skill in the art would have selected the compound modified as a "lead compound", which it defines as "a compound in the prior art that would be 'most promising to modify in order to improve upon its . . . activity and obtain a compound with better activity'. 890 F.3d 1328. (Pet.App.) *See Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1291 (Fed. Cir. 2012), citing *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). This standard creates a special obviousness standard for pharmaceutical compounds that is inconsistent with the most basic principles of the patent law of obviousness.

A. The Lead Compound Analysis Fails to Apply an Objective Analysis to Determine Obviousness

The Supreme Court standard of obviousness is objective[4]: It compares the scope and content of the prior art to the content of the claims and then considers

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[4] The analysis is objective: "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. Against this background the obviousness or nonobviousness of the subject matter is determined." *KSR*, 550 U.S. at 406

any differences between what the prior art teaches and what is claimed in the patent. By contrast, the lead compound theory is fundamentally a subjective judgment about what a hypothetical person of ordinary skill would prefer to "select" to develop, rather than an objective comparison of what the prior art teaches versus what is claimed. Whether a claimed invention is obvious depends objectively on what the person of ordinary skill in the art would have known—*i.e.* is the claim a new or nonobvious idea—and not on what a person of skill might select from information already known in the prior art.

What the art teaches is an objective fact—*e.g.*, a known compound is taught to have some utility and can be modified in a certain way—and that teaching can be objectively compared to what is claimed. What a hypothetical person of ordinary skill might "select" to develop as "most promising" to lead to a "better" compound is a subjective conclusion drawn by the court without criteria. Is the "most promising" compound the one with the most potent action? The one that is the least toxic? The one with the longest half-life? The one easiest to administer? The one easiest to make? In this case, for example, the court found that the most potent FAA compound in the prior art was not the "most promising".[5] The lead compound

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[5] Prior art FAA compounds named "2a" and "3a", exemplified in the '729 patent, were identical structures except that 3a had a nitrogen atom attached to the alpha carbon and 2a had a carbon atom attached there. The 2a and 3a compounds were essentially equivalent in activity. [Appx.747-748] Lacosamide (the R-stereoisomer of 107e) is compound 2a with the methoxy group added to the carbon on the alpha carbon. When a methoxy group was added to the analogous 3a compound at the nitrogen atom on

analysis has no standards that can be objectively applied. What is "most promising" can be anything the court choses, and any patentee's expert witness, using hindsight to avoid selecting what has been claimed in the patent, will always find something other than the claimed invention that the hypothetical person of ordinary skill in the art would arguably have selected as more promising to pursue.

B. The Lead Compound Analysis Fails to Compare the Claimed Invention to the Full Scope of the Prior Art

The lead compound analysis fails to compare the claimed invention to the scope and content of all of the prior art as required by both 35 U.S.C. § 103(a) and this Court's standard. That error is plainly illustrated here where the district court found that the only difference between the prior art compound 107e and the claimed compound (the R-stereoisomer of 107e) was an obvious one, but nonetheless eliminated 107e from consideration as prior art to compare to the claimed invention by concluding it would not have been selected as the lead compound.

The error is further illustrated by the Federal Circuit's affirming the conclusion that no FAA compound would have been selected as a "lead compound", 890 F.3d at 1322. (Pet.App.26a). Therefore, applying that theory, no FAA compound could have been obvious, despite considerable literature describing the FAA anticonvulsant compounds and a detailed

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the alpha carbon, the activity increased ten-fold, leading to the most potent FAA compound (named 3L) identified in the prior art. [Appx.744]

patent (the '729 patent) describing numerous specific FAA compounds as good anticonvulsants, disclosing a general formula for FAA anticonvulsant compounds, and teaching how FAA compounds could be modified to make other compounds with the same activity. The Federal Circuit lead compound analysis essentially removed the entire teaching about FAA anticonvulsants from prior art that could be compared to the patent's claims.[6]

In *KSR*, this Court rejected as a matter of law the suggestion that only modification of the best prior art could be obvious. There, the Court rejected as immaterial the assertion that one prior art reference would not have been used in the combination claimed because it was allegedly inferior compared to the inventor's preferred embodiment. *KSR*, 550 U.S. at 425. That holding cannot be reconciled with the lead compound analysis which holds that only the most promising compound could have an obvious modification.

The Federal Circuit precedent in other technologies is inconsistent with the lead compound analysis and is in accord with the holding of *KSR* that obviousness can be based on modification of prior art deemed inferior. *See In re Gurley*, 27 F.3d 551, 553 (Fed. Cir. 1994) ([Epoxy based printed circuit material] "[A] known or obvious composition does not become patentable simply because it has been described as some-

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[6] The Federal Circuit in *Otsuka* similarly excluded the entire class of carbostyril antipsychotic compounds from possible lead compounds precluding a conclusion that any new compound of that class could be obvious regardless of its close relation to or specifically taught modification of a prior art compound. 678 F.3d at 1289.

what inferior to some other product for the same use."); *In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004) ([Improved shoe sole] "The question is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination, not whether there is something in the prior art as a whole to suggest that the combination is the most desirable combination available.") (citation omitted). *In re Mouttet*, 686 F.3d 1322, 1334 (Fed. Cir. 2012) ([computing device] "[J]ust because better alternatives exist in the prior art does not mean that an inferior combination is inapt for obviousness purposes."). For reasons never articulated, the Federal Circuit no longer applies the same rule to pharmaceutical compounds.

C. The Lead Compound Analysis Conflicts with En Banc and Other Federal Circuit Precedent Concerning Obviousness of Compounds

The lead compound theory also conflicts with *en banc* precedent of the Federal Circuit regarding the standard of obviousness of chemical compounds. *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990) (*en banc*), confirms that obviousness of a claimed compound is determined by an objective comparison to any compound with a suggested utility in the prior art, not only those that are most promising to lead to an improvement. In that case, the applicant claimed a composition of a tetra-orthoester in a hydrocarbon fuel which had the property of reducing particulate emissions. The Federal Circuit held that the composition (which was governed by the same law as applied to compounds, *Id.* at 693 n.3) was obvious over a series of tri-orthoesters. The tri-orthoesters had been known

as useful water scavengers in hydrocarbon fuels, and a tetra-orthoester was shown to have water scavenging properties in a hydraulic fluid. The *en banc* court held that the composition was obvious, because a person of ordinary skill in the art would have been motivated to make tetra-orthoesters similar to the tri-orthoesters with the expectation that they would also be water scavengers in hydrocarbon fuels. The tri-orthoester could not have been the "most promising" "lead compound" to make a "better" emission reducing agent, because that property was unknown in the prior art tri-orthoesters which rendered the claimed composition obvious. Rather, as the *en banc* Federal Circuit held, the new compound was obvious because the modification was close in structure to the prior art compounds and a person of ordinary skill would have had a reasonable expectation that it would have a similar property—not necessarily better or improved—as the prior art compounds.

See also In re Lamberti, 545 F.2d 747, 751 (C.C. P.A. 1976) (A claimed compound was obvious based on its similarity to prior art compounds, even though the claimed compound was not of the type that the prior art had described as preferred).

The lead compound analysis adds an irrelevant obstacle to finding obviousness, in addition to the previously rejected Federal Circuit requirement that the prior art literally "teach, suggest or motivate" the claimed invention. *KSR Int'l v. Teleflex, Inc.,* 550 U.S. 419 (2007). Even when, as in this case, the prior art expressly teaches, and certainly suggests the invention, the lead compound analysis further requires that it also be proven that the prior art compound would

have been selected as the most promising compound to lead to one with better activity.

D. The Lead Compound Analysis Improperly Restricts the Type of Motive That Could Lead to the Invention

In re Dillon, and the case law cited therein, holds that a motivation to make a close or suggested structural modification of a compound with a known utility follows from the expectation that the new compound would have a similar utility. The motivation is lacking only where the prior art compound has no suggested utility at all. 919 F.2d at 697. This court also held in *KSR* that any motive, not merely the named inventor's, would suffice to support obviousness. 550 U.S. at 419-420. Contrary to *KSR* and *Dillon*, the lead compound analysis restricts consideration of motive to that likely to be held by a commercial company seeking to develop an improved commercial drug compound.

E. The Lead Compound Analysis Is Inconsistent with the Requirements for Patenting a Pharmaceutical Compound

The lead compound analysis is also inconsistent with the requirements for obtaining a patent on a pharmaceutical compound. To have patentable utility, a compound need not be better than other known compounds or be commercially useful, but rather need only have some pharmacological activity. *Nelson v. Bowler*, 626 F.2d 853, 856-58 (C.C.P.A. 1980); *Cross v. Iizuka*, 753 F.2d 1040, 1048 (Fed. Cir. 1985). Under the lead compound theory, the same evidence that would be sufficient to support the issuance of a patent

claim to a pharmaceutical compound would, if in the prior art, not be sufficient to show that the same patent claim was obvious.

CONCLUSION

There is no objective difference between what the prior art taught and the claims of the '551 patent. The patent adds no new idea to the art, but rather removes from public use concepts that were literally taught by the prior art. Applying the controlling Supreme Court standard, the claims of the '551 patent are obvious.

For the foregoing reasons, the petition for certiorari should be granted.

Respectfully submitted,

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