No. 18-441

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

AMICUS BRIEF ON BEHALF OF ASSOCIATION FOR ACCESSIBLE MEDICINE IN SUPPORT OF PETITIONER ACCORD HEALTHCARE SEEKING GRANT OF PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Whether the Federal Circuit can ignore this Court's precedent in *KSR v. Teleflex* by requiring a special and subjective "lead compound" test for invalidating chemical compounds, whereas all other types of patents are invalidated by the prior art as a whole.

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INTEREST OF *AMICUS CURIAE*[1]

The Association for Accessible Medicines ("AAM") is a nonprofit, voluntary association representing the interests of the generic and biosimilar medicines industry. AAM represents manufacturers and distributors of finished generic and biosimilar pharmaceuticals, manufacturers and distributors of bulk active pharmaceutical ingredients, and suppliers of other goods and services to the generic and biosimilar pharmaceutical industry. Its members provide Americans with generic and biosimilar medicines that are as safe and effective as their brand-name counterparts, but are substantially more affordable. In 2017, generic medicines accounted for roughly 90% of all prescriptions dispensed in the United States but only 23% of total spending. Generic medicines saved patients, taxpayers, and health care payers over $265 billion in 2017 compared to their brand-name counterparts.

AAM seeks to provide courts with the perspective of the generic and biosimilar pharmaceutical industry on important legal issues impacting its members, and to highlight the potential industry-wide consequences of significant pending cases.

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[1] Counsel for all parties do not object to the filing of this brief, in response to notice provided ten days prior to this filing. Pursuant to this Court's Rule 37.6, *amicus* states that this brief was not authored in whole or in part by counsel for any party, and that no person or entity other than *amicus curiae* or its counsel made a monetary contribution intended to fund the preparation or submission of this brief.

AAM's members are frequently involved in pharmaceutical patent litigation in which they rely on invalidity defenses such as obviousness of compound patents. Invalid patents undermine the legitimacy of the patent system, stifle competition, and impede consumers' access to low-cost medicines. AAM members have a significant interest in ensuring that statutory limits to the patent monopoly are enforced according to their terms.

SUMMARY OF ARGUMENT

Patient access to more affordable generic and biosimilar medicines may be thwarted by approval of pharmaceutical patents that are invalid due to lack of innovation. Patents covering branded medicines are typically challenged on various invalidity theories. One such theory relates to "obviousness" whereby a patent is declared invalid if the invention is non-existent or trivial based on the prior art. 35 U.S.C. § 103(a) (2012). This Court has set forth an objective standard for determining obviousness: (i) determining the scope and content of the prior art; (ii) comparing the differences between the prior art and the claims at issue; (iii) evaluating the level of ordinary skill in the pertinent art; and (iv) assessing objective evidence of nonobviousness. *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (citing *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966)). There is no separate requirement in this test to also prove that a particular prior art disclosure would have been recognized, ***subjectively*** or otherwise, as the "best" or "closest" or "lead" disclosure. Rather, the claims of a patent are ***objectively*** compared to the prior art as a whole.

Nevertheless, in the case of chemical compounds alone, the Court of Appeals for the Federal Circuit applies a different standard for obviousness. The Federal Circuit's obviousness standard for chemical compounds—commonly referred to as the "lead compound" analysis—is far more subjective and adds a step. The lead compound analysis inserts an additional step that requires a patent challenger to show that a chemist of ordinary skill would have already known from the prior art that the "lead compound" would be selected for further developed over other alternatives. Only then are the other steps of this Court's analysis applied, to determine the differences between the lead compound and the claimed invention, and to evaluate those differences.

For example, assume that a prior art reference discloses ten chemical compounds, any of which could be further modified in an obvious way. The Federal Circuit's test requires first showing that a chemist of ordinary skill in the art would have specifically selected only one of those ten compounds over the others. Having determined that this one compound is superior to the alternatives, the Federal Circuit's test then asks whether a person of ordinary skill would depart from the so-called "most promising" compound by modifying it in the manner proposed. This artificial first step is not required by, and is inconsistent with, the statute and is not employed for patents in all technological fields. For example (to analogize it to *KSR*), a prior art reference that disclosed ten different cars would still render adding an otherwise obvious braking system to any of them obvious, without picking out one car or braking system in particular.

The lead compound extra step is an extra-statutory standard the Federal Circuit applies to avoid finding obvious patents invalid. It has the effect of unnecessarily blocking generic pharmaceutical drug entry and thus harms patients, taxpayers, and all others who are required to pay monopoly prices for prescription medicines due to invalid patents. In doing so, the Federal Circuit's standard creates a special obviousness standard for pharmaceutical compounds which is inconsistent with the patent laws. The appeal in *Accord* seeks to eliminate the "lead compound" extra step for invalidating compound patents as obvious, so that compound patents are treated like every other kind of patent.

The Federal Circuit's test also conflicts with this Court's case law about obviousness. For example, the "lead compound" step contravenes this Court's rulings that (a) the same rules should apply to all patent technologies and (b) *KSR* in particular which held that the obviousness comparison is to the prior art as a whole and does not require knowing ahead of time which prior art is best or closest. Additionally, the "lead compound" case law by the Federal Circuit has created a split between newer panels and the prior en banc opinion *In re Dillon*, 919 F.2d 688 (Fed. Cir. 1990), which held that structural similarity alone and a reasonable expectation of success is enough to show obviousness.

ARGUMENT

The "lead compound" analysis imposed by the Federal Circuit departs from this Court's precedent, the statutory scheme, and the Federal Circuit's own en banc precedent. *Certiorari* should be granted so that this Court can stop the Federal Circuit from retreating to its own rigid formulations of obviousness in this important area of patent law.

I. ELIMINATING INVALID PATENTS INCREASES PATIENT ACCESS TO AFFORDABLE GENERIC AND BIOSIMILAR MEDICINES

Accord's petition for a writ of *certiorari* is important not only because it identifies a critical legal error, but also because it heavily impacts the ability to bring more affordable prescription drugs to patients. Brand-name pharmaceuticals often rely on compound patents to maintain a monopoly; using the correct standard to weed out invalid patents is critical to the proper functioning of the generic drug system.

A. Generic and Biosimilar Medicines Save Money and Improve Patient Access to Critical Medicines

Congress has recognized the benefits offered by generic medicines, and it sought to encourage their introduction by enacting the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585, commonly known as the Hatch-Waxman Amendments. *See Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990) (Congress

sought "to enable new drugs to be marketed more cheaply and quickly"); *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir.) (purpose of Hatch-Waxman was "to get generic drugs into the hands of patients at reasonable prices—fast"), cert. denied, 502 U.S. 906 (1991). More recently, Congress sought to enhance pharmaceutical competition through the introduction of biosimilar medicines by enacting the Biologics Price Competition and Innovation Act, Pub. L. No. 111-148, Tit. VII, Subtit. A, 124 Stat. 804. *See generally Sandoz Inc. v. Amgen Inc.*, 582 U.S. ___, 137 S. Ct. 1664 (2017). Patient access to low-cost, high-quality generic and biosimilar medicines remains critically important today given the high cost of healthcare in the United States.

The principal difference between generic or biosimilar medicines and brand-name prescription drugs or biologic products is cost. Association for Accessible Medicines, *Generic Drug Access & Savings in the U.S.* 24 (2018) (*Generic Drug Access*). Generics account for 90% of prescriptions dispensed in the United States, but only 23% of total drug costs. *Id.* at 10. In total, generic medicines generated $265.1 billion in savings for the American healthcare system in 2017, and $1.79 trillion in savings over the last decade. *Id.* at 11. Generic medicines saved the Medicaid system $40.6 billion and saved the Medicare system $82.7 billion. *Id.* at 4.

The benefits of more affordable generic and biosimilar medicines extend beyond mere cost savings. Generic drugs reduce the problem of lack of adherence because new patients are three times less likely to stop taking generic medications than brand-name drugs. *Generic Drug Access* 16.

All of these benefits flow directly from the competition that generic and biosimilar medications provide to brand-name drugs that would otherwise enjoy monopoly status. The more competitors there are, the greater the savings: The entry of a second generic manufacturer into the market reduces the average generic price to nearly half the brand-name price, and for medicines that attract a large number of generic manufacturers, the average generic price falls to less than 20% of the branded price. U.S. Food & Drug Admin., *Generic Competition and Drug Prices* (May 13, 2015), http://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm129385.htm.

Not only is the generic marketplace good for patients, but it benefits taxpayers, too. Although brand-name drugs account for only 11% of prescriptions dispensed in the U.S., they account for more than 74% of total drug spending. One of the largest subsidizers of prescriptions is the federal government. *Generic Drug Access* at 33. In 2015, the U.S. government paid roughly 43% of all retail prescription drug costs—29% through Medicare and 10% through Medicaid. Peter Olson & Louise Sheiner, *The Hutchins Center Explains: Prescription Drug Spending*, Brookings Inst. (Apr. 26, 2017), https://www.brookings.edu/blog/up-front/2017/04/26/the-hutchins-center-explains-prescription-drug-spending/. Medicare and Medicaid saved $77 billion and $37.9 billion, respectively, in 2016 due to savings associated with lower-cost, generic drug options. Ass'n for Accessible Medicines, White Paper, *Ensuring the Future of Accessible Medicines in the U.S.*, at 6 (2018), http://accessiblemeds.org/sites/default/

files/2018-12/AAM-Whitepaper-Ensuring-Future-of-Generic-Medicines.pdf. This equates to an average annual savings of $1,883 per Medicare enrollee and $512 per Medicaid enrollee. *Id.* With health expenditures climbing 5.8% in 2015 and accounting for 17.8% of Gross Domestic Product, the savings associated with generic drug options has become an indispensable component of national health policy.

B. Invalid Patents Block the Introduction of More Affordable Generic and Biosimilar Medicines

Patent law "strikes a delicate balance between creating 'incentives that lead to creation, invention, and discovery' and 'imped[ing] the flow of information that might permit, indeed spur, invention.'" *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2116 (2013) (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 92 (2012)) (alteration in original). Especially in the pharmaceutical context, that balance is frequently upset by the assertion of invalid patents, which inevitably leads to lengthy and expensive litigation. Delay in removing improperly awarded patents can lead to substantially higher drug costs for patients, insurers, and taxpayers.

Congress's foray into prescription drug policy, however, has not deterred anti-competitive practices by some brand drug manufacturers. Such manufacturers may engage in a variety of practices known as "evergreening" that seek to extend a drug's period of exclusivity as a means of preventing low-cost alternatives from entering the market. For instance, they may attempt to "patent 'new inventions' that are

really just slight modifications of old drugs." Roger Collier, *Drug Patents: The Evergreening Problem*, 185 Can. Med. Ass'n J. E385, E385 (2013), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3680578/; *see generally* Scott C. Hemphill & Bhaven N. Sampat, *Evergreening, Patent Challenges, and Effective Market Life in Pharmaceuticals*, 31 J. Health Econ. 327 (2011). Such patents result in fresh 20-year monopolies on drugs that should be in the public domain. Alternatively, manufacturers may take advantage of a provision of the Hatch-Waxman Act staying generic entry for 30 months under certain circumstances, by securing seriatim stays that can delay generic entry indefinitely. Stacey L. Dogan & Mark A. Lemley, *Antitrust Law and Regulatory Gaming*, 87 Tex. L. Rev. 685, 711-15 (2009) (explaining this strategy in detail). Those practices inhibit innovation and harm the nation's fiscal health. So, too, does the Federal Circuit's "lead compound" test. Every obvious patent that cannot be efficiently invalidated in patent challenges, further delays entrance of generic drugs and harms consumers.

The propriety of the Federal Circuit's "lead compound" test is important for the Court to resolve because compound patents are listed for almost every approved drug on the market. Generic drug manufacturers have become disincentivized to challenge this type of patent because of the extra steps required by the Federal Circuit's overly rigid test. We will never know the extent of the damage because companies choose not to challenge compound patents in lieu of waiting for expiration of those patents. With the current incorrect standard, some companies choose not to challenge compound patents,

delaying access to cheaper medicines for millions of Americans.

II. THE FEDERAL CIRCUIT'S "LEAD COMPOUND" TEST REPEATS THE ERROR THAT LED TO THIS COURT'S RULING IN *KSR*

Despite this Court's guidance, the Federal Circuit has resorted to the use of overly restrictive obviousness paradigms, just as it had before *KSR*. In that case, this Court corrected the Federal Circuit's "teaching/suggestion/modification" test which required express instructions to make an invention obvious, even if the scientific community had well understood otherwise obvious changes to the prior art. Similarly here, the Court should correct the Federal Circuit's "lead compound" test which requires expressly showing a skilled artisan would have selected a specific compound for further development over other alternatives, even if the scientific community had good reasons to make obvious changes to the prior art.

A. In *KSR*, the Court Rejected the Federal Circuit's Rigid and Formulaic Approach to Obviousness

In 2007, this Court's decision in *KSR* clarified the standards for obviousness under 35 U.S.C. § 103. 550 U.S. 398. Before *KSR*, the Federal Circuit had adopted the "teaching, suggestion, or motivation" ("TSM") test to evaluate obviousness of a claimed invention in the prior art. *Id.* at 407. The Federal Circuit's TSM test erroneously required that the prior art expressly and explicitly disclose that two concepts

should be combined and that the combination would likely be successful. *Id.*

This Court rejected the Federal Circuit's "rigid approach" to obviousness as contrary to precedent. *Id.* at 415. In particular, the Court rejected the TSM test because it improperly narrowed the inquiry in *Graham*. *Id.* (citing *Graham*, 383 U.S. at 17–18). The TSM test may have begun as a helpful insight into the Court's reasoning, but it became a mandatory formula that arbitrarily and improperly restricted the obviousness inquiry. *Id.* at 418–19.

In *KSR*, the Court identified two critical errors in the rigid application of the TSM test. First, the Federal Circuit's analysis required that "courts and patent examiners should look only to the problem the patentee was trying to solve." *Id.* at 420. This was error because it transforms the objective question of obviousness into a subjective question particular to the patentee, rather than the scientific field at large. *Id.*

Second, the rigid TSM test treated even an objective person of ordinary skill in the art as lacking creativity or imagination, and requiring one express teaching rather than the ability to broadly apply established scientific knowledge as a skilled artisan would do. *Id.* at 420–21. The Federal Circuit test excluded prior art from a court's analysis unless it was designed specifically to solve the same problem as the claimed invention. *Id.* As the Court concluded, "[a] person of ordinary skill is also a person of ordinary creativity, not on automaton." *Id.* at 421.

The Court also found that these errors caused the Federal Circuit to reject wholesale that a patent claim could be proved obvious "by showing that that combination of elements was 'obvious to try.'" *Id.*

Ultimately, *KSR* clarified the approach for courts and examiners to use when evaluating obviousness.

> When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. ... [A] court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.

550 U.S. at 417. This approach is flexible and takes into account that "in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* at 420. It nowhere requires first knowing which "lead" prior art should be modified instead of alternative compounds, which is a subjective approach for assessing the prior art that is not used in other obviousness analyses. Rather, any obvious modifications of the prior art, whether "lead" or not, are obvious and not separately patentable.

B. The Federal Circuit's "Lead Compound" Test Repeats the Same Errors as the Rejected TSM Test

Since the decision in *KSR*, the Federal Circuit has fallen back into its old habits and created a rigid rule for chemical patents that unfairly narrows the obviousness inquiry. The "lead compound" test is overly rigid because it limits the scope and content of the prior art and treats the objective skilled artisan as an automaton. Tracing back the history of the test shows how the Federal Circuit got it wrong, and ignored this Court's precedent in the process.

1. As with TSM, the Federal Circuit transformed a potentially helpful insight into a rigid, extra-textual requirement

Early on, the Federal Circuit grappled with the question of how to determine the obviousness of chemical compounds. In 1990, the full Federal Circuit adopted a flexible standard for evaluating the obviousness of chemical compounds that required only structural similarity between the prior art and claimed compound and a motivation to make the claimed composition. *In re Dillon*, 919 F.2d 688, 692–93 (Fed. Cir. 1990) (en banc). The en banc panel summarized its holding:

> In brief, the cases establish that if an examiner considers that he has found prior art close enough to the claimed invention to give one skilled in the relevant chemical art the motivation to make close relatives (homologs, analogs, isomers, etc.) of the prior art

> compound(s), then there arises what has been called a presumption of obviousness or a *prima facie* case of obviousness.

Id. at 696. This holding permitted no separate requirement for an extra "lead compound" analysis.

The *Dillon* decision correctly presaged *KSR* by holding that the motivation to make the claimed compound need not be the same as the patentee's stated motivation:

> Each situation must be considered on its own facts, but it is not necessary in order to establish a *prima facie* case of obviousness that both a structural similarity between a claimed and prior art compound (or a key component of a composition) be shown and that there be a suggestion in or expectation from *the prior art* that the claimed compound or composition will have the same or a similar utility *as one newly discovered by applicant.*

Id. at 693 (emphasis in original); *see KSR*, 550 U.S. at 420 ("The first error of the Court of Appeals in this case was to foreclose this reasoning by holding that courts and patent examiners should look only to the problem the patentee was trying to solve."). In addition, the *Dillon* formulation represented the flexible nature of an obviousness inquiry and the breadth of the prior art: "There is no question that all evidence of the properties of the claimed compositions and the prior art must be considered in determining the ultimate question of patentability." *Dillon*, 919 F.2d at 693.

Indeed, in *Dillon* itself, the Federal Circuit affirmed patent invalidity because the prior art disclosed structurally similar compounds and "provided the motivation to make the claimed compositions in the expectation that they would have similar properties." *Id.* Again, there was no requirement to first select a lead compound before doing this further analysis.

A decade later, however, the Federal Circuit engrafted its rigid and extra-statutory TSM test into the flexible framework of *Dillon*, requiring one to first select a "lead compound" and planting the seeds of today's flawed test. *Yamanouchi Pharmaceutical Co. v. Merck & Co., Inc.*, 231 F.3d 1339 (Fed. Cir. 2000).

The *Yamanouchi* panel emphasized that evidence of teaching, suggestion, or motivation must be explicit in the prior art—a rule that *KSR* later reversed. *Id.* (quoting *In re Rouffet*, 149 F.3d 1350, 1357–58 (Fed. Cir. 1998)). In particular, the panel focused on the lack of explicit motivation to choose the identified lead compound for further work. *Id.* at 1344–45. In requiring the express motivation for a lead compound, the panel rejected the patent challenger's evidence that one prior art compound was "three times more active" than others, because there were also other active compounds. *Id.* at 1345. The panel concluded: "If activity alone was the sole motivation, other more active compounds would have been the obvious choices, not example 44 [the lead compound]." *Id.* The panel also separately found that the prior art would not have expressly motivated a person of skill in the art to make the multiple chemical manipulations required to transform the lead compound into the claimed compound. *Id.*

The Federal Circuit then restated its "lead compound" analysis years later in *Eli Lilly & Co. v. Zenith Goldline Pharmaceuticals, Inc.*, 471 F.3d 1369 (Fed. Cir. 2006)—just before this Court's rejection of the TSM test. In *Eli Lilly*, the panel correctly applied the *Dillon* test by noting that although the identified prior art was structurally similar, other evidence warranted a finding of non-obviousness. *Id.* at 1378. The panel relied on the district court's factual findings that the claimed compound had sufficient "unexpected beneficial properties" that overcame the evidence of obviousness. *Id.*

Then in *dicta*, the panel noted the similarities between its situation and that of *Yamanouchi* because a skilled artisan would not have chosen to start with the identified prior art compound. *Id.* at 1378–79. The discussion of *Yamanouchi* in *Eli Lily* was not dispositive to the decision, but supported the unremarkable proposition that "mere identification in the prior art of each component of a composition does not show that the combination as a whole lacks the necessary attributes for patentability, i.e. is obvious." *Id.* More specifically, the evidence that prior art taught against using the identified compound in any combination (whether or not a "lead") negated the defendants' evidence of motivation to combine the prior art. *Eli Lilly* should not have been read to require a separate motivation to choose a "lead compound" distinct from the motivation to combine prior art. *Id.*

Unfortunately, the Federal Circuit later transformed the distracting insight in *Eli Lilly* into a strict requirement for an explicit motivation to choose a particular lead compound: "Thus, in cases involving

new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1356–57 (Fed. Cir. 2007) (discussing the "lead compound" test after *KSR*).

In *Takeda*, the panel further distanced itself from the *Dillon* "structural similarity" test in favor of the overly exacting "lead compound" test. As noted by the panel, *Dillon* should control the inquiry (*id.* at 1356), so defendants should only have been required to establish (1) a showing of structural similarity and (2) "suggestion in or expectation from *the prior art* that the claimed compound or composition will have the same or a similar utility *as one newly discovered by applicant*." *Dillon*, 919 F.2d at 693 (emphasis in original). There was no dispute that the prior art compound was a structural homologue to the claimed compound. But for the second step, rather than confirm that the "utility" was similar between the prior art compound and the patented one, the panel instead analyzed whether the prior art compound would have been selected in the first place. According to the panel, the patent challenger had to show that prior art compounds selected from within a reference were "the best performing compounds as antidiabetics, and hence targets for modification to seek improved properties." 492 F.3d at 1357. In other words, the *Takeda* panel purportedly changed the en banc rule from *Dillon*: rather than merely show utility, the patent challenger had to show a lead compound was among the best of all possible alternatives. *See id.* As further support for its

position, the panel disregarded a second prior art reference that called out the lead compound as of particular interest for further development because some tests showed it caused side effects. *Id.* at 1358. Again, the panel emphasized that the prior art could not form the basis for obviousness because it was not the "*best candidate* as the lead compound" option for modification. *Id.* (emphasis added).

The *Takeda* panel attempted to square its analysis with *KSR*, but wrongly focused on whether the lead compound was obvious, rather than whether the changes to the prior art were obvious. According to the panel, "[r]ather than identify predictable solutions for antidiabetic treatment, the prior art disclosed a broad selection of compounds any one of which could have been selected as a lead compound for further investigation." *Id.* at 1359. This version of the test starts by asking about "predictable solutions"—which should have focused on what changes would be made—but instead required there to have been one "lead compound." Under *Takeda*, therefore, if a prior art reference did not identify a lead compound as superior to alternatives, then any changes to it could not be obvious. This rule directly contradicts *KSR*, which focused on what changes would be made based on the prior art as a whole.

After *Takeda*, the Federal Circuit treated the "lead compound" test as settled precedent, and spread the flawed logic. For example, in *Eisai*, a panel rejected a potential lead compound that was 20 times better than the best-selling anti-ulcer medicine because of potential side effects. *Eisai Co. Ltd. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1358 (Fed. Cir. 2008) (citing *Takeda*, 492 F.3d at 1359). The *Eisai* panel

referenced the *Takeda* panel's distinguishing of *KSR* to conclude that "post-*KSR*, a prima facie case of obviousness for a chemical compound still, in general, begins with the reasoned identification of a lead compound." *Id.* at 1359. The *Eisai* panel makes no reference to the flexible standard of *Dillon*, entirely substituting the "lead compound" standard of *Takeda*. *See id.*

This formulation of the "lead compound" test has become calcified in subsequent decisions by the Federal Circuit. *E.g.*, *Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1291 (Fed. Cir. 2012) (requiring a lead compound "be most promising to modify" and analyzing the compound based on pertinent properties instead of structural similarity); *In re Rosuvastatin Calcium Patent Litig.*, 703 F.3d 511, 518 (Fed. Cir. 2012) (finding the identified, structurally similar compound not a "lead compound" because the prior art considered other prior art compounds more promising); *Pfizer Inc. v. Teva Pharms. USA, Inc.*, 555 F. App'x 961, 969 (Fed. Cir. 2014) (requiring selection of a "most promising" lead compound not based on structural similarity). In the only case where a compound has been found to be obvious, the panel found the identified lead compound acceptable because the patent owner's own expert admitted it had already been selected for further development by other researchers. *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 974 (Fed. Cir. 2014).

In sum, the *Takeda* panel's "lead compound" test is derived from *dicta* from a pre-*KSR* case that does not require the selection of a "best candidate"

(*Eli Lilly*) and a pre-*KSR* case that requires the now-rejected TSM test (*Yamanouchi*).

2. The "lead compound" test repeats the errors this Court rejected in *KSR*

The "lead compound" test of *Takeda* and its progeny is effectively just another spin on the same rigid TSM test specifically rejected in *KSR*. This Court admonished the Federal Circuit for its "narrow conception of the obviousness inquiry reflected in its application of the TSM test." *KSR*, 550 U.S. at 419. The Court should grant *certiorari* to rectify the Federal Circuit's narrow conception of the obviousness inquiry in chemical patent cases.

The "lead compound" analysis is uniquely applied to chemical compounds, and not used to evaluate the obviousness of other types of patents. In *KSR*, the Court properly focused the analysis on what a person of ordinary skill in the art would know and would be motivated to make from the prior art disclosures. *Id.* at 425. The Court did not require that the prior art starting point was the best, most advanced, or least problematic gas pedal. *KSR*, 550 U.S. at 424–25. In fact, this Court noted that no singular appropriate starting point exists—a person of skill in the art could either try to adapt an off-the-shelf analog pedal (Asano), or could try to improve an electronic pedal (Rixon). *Id.* The identification of two potential lead references was not a reason to stop the inquiry and conclude that a skilled artisan would simply give up. And even with evidence that the Asano pedal was not the most efficient analog pedal in the prior art, still it

could be used as the basis for obvious modifications that a person of skill in the art would pursue.

A related problem with the Federal Circuit's approach is that the Federal Circuit sometimes states that there can be more than one lead compound. For example, the *Altana* panel reasoned that so long as it did not require the selection of a single "lead compound" then the test would not run afoul of *KSR*. *Altana Pharma AG v. Teva Pharms. USA, Inc.*, 566 F.3d 999, 1008 (Fed. Cir. 2009). But district court judges are even more confused by that approach: if there are two possible lead compounds, then a judge may simply conclude there is no "best" lead compound. *See Takeda*, 492 F.3d at 1358; *Eisai*, 533 F.3d at 1358.

The "lead compound" analysis engages in impermissible hindsight analysis. In reality, where a prior art reference discloses a set of related compounds, the reference renders obvious numerous structurally related analogs made by making obvious changes that would have been obvious in light of the prior art. But the "lead compound" analysis pretends that none of these otherwise obvious resulting compounds are invalid except the one that the inventor chose for further development. This is not only a subjective test, but it also ignores that more than one compound can be obvious. In *KSR*, this exact approach—arguing that prior art Asano was less efficient than the claimed pedal—was rejected because it "would be to engage in the very hindsight bias Teleflex rightly urges must be avoided." *KSR*, 550 U.S. at 426. The "second best" prior art compound may have obvious modifications and analogues that end up more effective than modifications to the "best"

prior art compound. This does not mean that those analogues, obvious to a person of skill in the art, should not also be obvious to a finder of fact.

Finally, the "best candidate" approach of *Takeda* ignores the reality of modern chemical synthesis. Chemical compounds are routinely synthesized and screened for activity. For years now, companies have pursued combinatorial chemistry and "high throughput screening" where thousands of analogues can be examined simultaneously and quickly screened for efficacy. In that way, even patent owners do not first select a "best candidate," but instead look at various interesting structures and make changes to them, some of which are obvious. Today's drug discovery relies on structural similarity, but the Federal Circuit has rejected this approach.

CONCLUSION

As the foremost treatise on Patent Law notes, the Federal Circuit's further development of a lead compound test post-KSR is "ironic because *KSR* was critical of any 'rigid' application of a suggestion test and was [*sic*] been generally understood as stabilizing or even raising the patentability bar, not lowering it." Donald S. Chisum, 2 CHISUM ON PATENTS § 5.04B[6][d].

The Court should grant Accord's petition for a grant of *certiorari* to correct the Federal Circuit's legally erroneous "lead compound" test and replace it with the statutory obviousness test of comparing the claimed invention to the prior art as a whole.

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