No. 18-817

In the Supreme Court of the United States

HIKMA PHARMACEUTICALS USA INC., AND WEST-WARD PHARMACEUTICALS INTERNATIONAL LTD., N/K/A HIKMA PHARMACEUTICALS INTERNATIONAL LTD., PETITIONERS

v.

VANDA PHARMACEUTICALS INC., RESPONDENT

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

REPLY TO BRIEF IN OPPOSITION

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The Rule 29.6 Statement included in the petition for a writ of certiorari, as updated by the brief in opposition for respondents, remains accurate.

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REPLY TO BRIEF IN OPPOSITION

Vanda's opposition rests on the premise that this case is a poor vehicle to decide the question presented because the decision below does not adopt a "categorical" rule for "method-of-treatment claims," but rather is "fact-specific" and limited "to just the '610 patent." Opp. 1, 21, 36. That premise is false.

The Federal Circuit "distin[guished] between method of treatment claims and those in *Mayo*." App. 32a. The dissent highlighted that distinction. App. 49a. Of the fifteen later Federal Circuit cases that Vanda cites, just two involved life science patents, and those decisions double down, "underscor[ing] the distinction between method of treatment claims and those in *Mayo*." *CEPHEID*, 905 F.3d at 1373 n.7; see *Athena Diagnostics, Inc.* v. *Mayo Collaborative Servs.*, 2019 WL 453489, *6 (Fed. Cir. Feb. 6, 2019).

Likewise, the Patent Office has told its examiners "how to evaluate the patent eligibility of 'method of treatment claims' in light of [the] decision": "Method of treatment claims (which *apply* natural relationships as opposed to being 'directed to' them)" are not "implicated by" §101. App. 98a, 99a. Full stop.

The Court need not take our word for it, however. As Vanda's counsel publicly announced, the ruling is a "landmark decision" with "broad implications."[1] Counsel acknowledged that those implications extend

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[1] *Landmark Decision for Vanda Affirms that Innovations in Treatment Can Be Patented*, Paul Weiss (April 13, 2018), https://www.paulweiss.com/practices/litigation/ip-litigation-patent/news/landmark-decision-for-vanda-affirms-that-innovations-in-treatment-can-be-patented?id=26270.

not only to "personalized medicine," but "frankly [to] patents on methods of treatment as a whole."[2]

Counsel's out-of-court statements are correct. As confirmed by 22 academic, nonprofit, and industry *amici*—including seventeen patent-law professors—the decision below purports to "categorically exclude[] every method-of-treatment claim" from §101 scrutiny. IP Profs. Br. 7; accord AAM Br. 6. And commentators continue to agree that, in "a sharp break from post-*Mayo* decisions," the decision purports to hold "method of treatment claims per se patent-eligible."[3]

Once it becomes evident that the decision below is not "fact-specific," little remains of the opposition. Vanda says its "claims are patent eligible under this Court's precedent" (Opp. 22–31)—which the Federal Circuit "faithfully applied" (Opp. 12–21)—because Vanda claimed "a new way of using an existing drug" (*Mayo*, 566 U.S. at 87). Yet Vanda admits that "iloperidone was known to treat schizophrenia." C.A. App. 10234. Vanda also says its claims satisfy step one of *Mayo* simply because they "apply" natural laws (Opp. 12–30), but §101 requires more than "an instruction to doctors to apply the applicable laws when treating their patients." *Mayo*, 566 U.S. at 79.

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[2] *Life Sciences Group of the Year: Paul Weiss*, Law360 (Jan. 16, 2019), https://www.law360.com/articles/1113883/life-sciences-group-of-the-year-paul-weiss.

[3] Hedemann & Ludwig, *Method-of-Treatment Patent Eligibility: Step 1 and Done?*, Law360 (Feb. 5, 2019), https://www.law360.com/ip/articles/1125488/method-of-treatment-patent-eligibility-step-1-and-done-.

We address Vanda's merits arguments below, but they can be considered in depth if the Court grants certiorari. As Vanda admits, "an enormous number of patents" claim treatment methods, and "thousands" are listed in the Orange Book. Opp. 10, 33. That means they can trigger "30-month stays of FDA approval for generic drugs" (Opp. 10)—a multi-billion-dollar industry that doctors and patients depend on daily. However the merits are ultimately resolved, certiorari is warranted.

I. The decision below broadly exempts method-of-treatment claims from Section 101 scrutiny—even if they apply a natural law using only routine and conventional steps.

A. As Vanda acknowledges, the court below held that Vanda's claims "are not 'directed to' a law of nature at Step One" of the *Mayo/Alice* framework—and thus never reached "Step Two," which requires more than "routine and conventional" activity. Opp. 30. That ruling is not limited to "the '610 patent." Opp. 1.

As the court below explained, the *reason* it believed Vanda's claims were not "directed to" natural laws is that they are instead "directed to a novel method of treating a disease." App. 31a. That logic applies to every patent that claims a "method of treating a disease." *Ibid.*

Far from disclaiming that result, the court repeatedly "distin[guished] between method of treatment claims and those in *Mayo*." App. 32a. Over and over, the court distinguished *Mayo* on those grounds:

- The claim there "was not directed to the application of a drug to treat a particular disease."

- The "claim [there] was not a treatment claim," while Vanda claims "treatment steps."
- This case is "different from *Mayo*" because Vanda claims "a method of treating patients."

App. 31a–33a, 35a. None of this reasoning is "fact-specific." Opp. 36.

B. Nor did the dissent below "differ[] only as to the outcome." Opp. 1. Chief Judge Prost directly addressed the majority's sweeping rule for method-of-treatment claims: "Whatever weight can be ascribed to the foregoing statements *about methods of treatment*, we remain beholden to the holding of *Mayo*." App. 49a (emphasis added). She also objected that the majority "d[id] not heed [*Mayo*'s] warning" "against drafting efforts designed to monopolize the law of nature itself." App. 47a (quotation omitted). The decision invites patentees to do exactly that—by reciting generic treatment steps that "simply direct the relevant audience to apply it." App. 44a.

C. None of the fifteen decisions in which the Federal Circuit has since "held patent claims to be *ineligible*" (Opp. 20–21) involved method-of-treatment claims, and just two involved life sciences. *CEPHEID* describes the decision below as "underscor[ing] the distinction between method of treatment claims and those in *Mayo*." 905 F.3d at 1373 n.7. And *Athena* describes it as holding that "claiming a new treatment for an ailment, albeit using a natural law, is not claiming the natural law." 2019 WL 453489, *6.

D. Vanda's "fact-specific" framing is also belied by the Patent Office's reading. According to Vanda, the PTO "says only that method-of-treatment claims that 'apply' natural relationships, 'as opposed to being 'di-

rected to' them,' are eligible for patenting." Opp. 11. That is a verbal sleight of hand.

In passages not cited by Vanda, the PTO's *Vanda* Memo quotes the decision as "'underscor[ing] the distinction between method of treatment claims and those in *Mayo*'" and broadly directs examiners that "[m]ethod of treatment claims (which *apply* natural relationships as opposed to being 'directed to' them)" are not "implicated by" §101. App. 98a (quoting App. 32a). In other words, method-of-treatment claims by definition "apply natural relationships as opposed to being 'directed to' them." *Ibid*. That is why the PTO requires finding such claims "patent eligible" even if they "include nonroutine or unconventional steps." App. 98a–99a.

Vanda cites recent guidance for patents generally, noting that the PTO invited public comment. Opp. 34. But nothing in that guidance retreats from the *Vanda* Memo, which comprehensively addresses "how to evaluate the patent eligibility of 'method of treatment claims' in light of" the decision below. App. 99a.

E. Since the petition *and* the PTO's general guidance, even more commentators have weighed in. All agree that the PTO has "directed its examiners to hold method of treatment claims eligible * * * without even considering whether the claims contain any nonroutine or unconventional" steps. Hedemann, *supra*. That instruction flows from the decision below, which purports to render "method of treatment claims per se patent-eligible." *Ibid*. Now, provided a "claim has any kind of treatment element to it, it's

going to survive"[4]—and drafting that step requires just a "simple tweak."[5]

Even Vanda's counsel agrees—outside of court—that the decision below is a "landmark decision" with "broad implications," including "for patents on methods of treatment as a whole." *Supra* nn. 1–2.

II. Vanda's merits arguments are incorrect and do not diminish the need for review.

The balance of Vanda's brief largely presses merits arguments that its claims "are patent eligible under this Court's precedent" (Opp. 22–31), which the Federal Circuit purportedly "faithfully applied" (Opp. 12–21). These arguments are not plausible, but would not seriously undermine the case for certiorari even if they were.

A. Vanda cannot rehabilitate the majority's holding that all methods of treatment are patent-eligible "applications."

1. Echoing the court below, Vanda says its claims satisfy step one of *Mayo/Alice* simply because they recite "an *application* of a law of nature." Opp. 29 (quotation omitted). Provided a claim "*applies* a law of nature," Vanda insists, "Step Two scrutiny is [not]

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[4] Davis, *3 Takeaways from the Latest Ax of a Diagnostic Patent*, Law360 (Feb. 12, 2019), https://www.law360.com/ip/articles/1128379/3-takeaways-from-the-latest-ax-of-a-diagnostic-patent.

[5] Marsili, *Federal Circuit Skips the Mayo in Upholding Vanda's Fanapt® Patent*, Carlson Caspers (April 26, 2018), https://www.carlsoncaspers.com/federal-circuit-skips-the-mayo-in-upholding-vandas-fanapt-patent/.

required," and courts need not ask whether the application is "routine and conventional." Opp. 18, 30. Notably, this view applies to *all* method-of-treatment claims—not just Vanda's. But it is mistaken.

This Court has never held that any "application" confers eligibility. *Funk Brothers* invalidated "an application of [a] newly-discovered natural principle" (333 U.S. at 131–132), and *Flook* held that "usefully appl[ying]" an equation did not pass muster either. 437 U.S. at 590. As *Mayo* explained, §101 requires "more than simply stat[ing] the law of nature while adding the words 'apply it.'" 566 U.S. at 72. Indeed, the notion that any "application" is sufficient resurrects an argument unanimously rejected there—that "virtually any step beyond a statement of a law of nature itself should transform an unpatentable law of nature into a potentially patentable application," which "would make the 'law of nature' exception to §101 patentability a dead letter." *Id.* at 89.

2. Recasting natural laws as "methods of treatment" violates these principles. In the medical arts, patentees can add treatment to any claim. That is just "an instruction to doctors to apply the applicable laws when treating their patients," which "add[s] nothing specific." *Id.* at 79, 82. Generic "administering" and "determining" steps are not "sufficient to transform the nature of the claim." *Id.* at 78.

Generic "treatment" is no different. IP Profs. Br. 6–9; AAM Br. 9–12. If anything, the patent in *Mayo* recited a *more specific* application than the "method of treatment" here—it required "[a] method of optimizing therapeutic efficacy for treatment." 566 U.S. at 74–75. The patent thus "claimed processes"—putative applications of the relevant natural laws—

but not "transform[ative]," and thus "patent-eligible, applications of those laws." *Id*. at 72.

Contrast Morse's "telegraph machines." Opp. 13. This Court did not find them patentable just because they "applied" natural laws. It reaffirmed *O'Reilly*'s holding that mere "use of magnetism as a motive power * * * could not be claimed." *Dolbear* v. *American Bell Co.*, 126 U.S. 1, 534 (1888). This time, however, Morse claimed a machine that transformed that power. And "without this peculiar change in its condition it will not serve as a medium for the transmission of speech, but with the change it will." *Ibid*. That "peculiar change"—not the generic "use" of electromagnetism—made Morse's machine patentable.

3. According to Vanda, we "want[] this Court to hold that all method-of-treatment patents are *in*eligible." Opp. 11–12. That is a straw man. Treatment methods can be patentable. Pet. 21–22. The question is what it takes for them to satisfy §101. And "a process reciting a law of nature" is invalid "unless [it] has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature." *Mayo*, 566 U.S. at 77. Simply redrafting natural laws as "methods of treatment" provides no such assurance.

B. Vanda cannot distinguish its claims from those struck down in *Mayo*.

Once it becomes clear that reciting a method of treatment does not, without more, guarantee the patentee success at step one of *Mayo/Alice*, it becomes equally clear that Vanda's claims are invalid.

1. At the first step, Vanda cannot seriously dispute that its claims "set forth laws of nature." *Mayo*, 566 U.S. at 77. They divide patients into two

groups—those with a "CYP2D6 poor metabolizer genotype" and those without it—and recite that those with the genotype should take reduced doses to decrease their "risk of QTc prolongation," whereas those without the genotype should take normal doses. App. 3a–4a. That "simply discloses the natural law that a known side effect of the existing treatment could be reduced by administering a lower dose" to high-risk patients. App. 48a (Prost, C.J., dissenting).

That is materially the same as the natural law in *Mayo*—a correlation "between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." 566 U.S. at 77. Here the drug is iloperidone, not thiopurine, and the diagnostic is a genotype, not a blood level. But the natural law is otherwise identical—a correlation "between [a patient's genotype] and the likelihood that a dosage of a[n] [iloperidone] drug will prove ineffective or cause harm." *Ibid.* Because Vanda's claims are "directed to" that natural law, they fail step one.

2. Vanda tries to distinguish *Mayo* based on the claims' alleged specificity—they are "limited to iloperidone" and "require doctors to give specific dosages" to "specific patient populations." Opp. 6, 10. As explained below, the claims in *Mayo* were, if anything, more specific. More fundamentally, however, Vanda "conflates the inquiry at step one with the search for an inventive concept at step two." App. 43a (Prost, C.J., dissenting). "Once the natural law claimed in the '610 patent is understood in a manner consistent with *Mayo*," step one is over—the question becomes whether, under step two, the claims "supply the requisite inventive concept to transform the natural law into patent-eligible subject matter." *Ibid.*

a. Even if they were relevant at step one, Vanda cannot distinguish its so-called "specific" elements from the elements in *Mayo*.

First, that the claims are "limited to iloperidone" is irrelevant. Opp. 6. The claims in *Mayo* were likewise limited to "a thiopurine drug." 566 U.S. at 77.

Second, the claims are not directed to "specific patient populations." Opp. 10. They cover *all* schizophrenia patients and simply divide them into two groups based on "genotype." App. 3a–4a. Those "populations" are as broad as *Mayo*'s, which likewise included all "immune-mediated gastrointestinal disorder" patients and divided them by "level[s] of 6-thioguanine." 566 U.S. at 74–75.

Third, the claims are not directed to "specific dosages." Opp. 10. Poor metabolizers receive a reduced dosage of "12 mg/day *or less*," while every other patient receives a conventional dosage "*greater* than 12 mg/day, up to 24 mg/day." App. 4a (emphasis added). Again, the claims track those in *Mayo*, which stated that low metabolite levels "indicate[] a need to increase" the dosage and higher levels "indicate[] a need to decrease" it. 566 U.S. at 75.

b. For the same reasons, these elements contribute no "inventive concept" at step two. *Alice*, 573 U.S. at 217. Below, only the dissent reached that issue, correctly concluding that the claims recite "no more than instructions * * * to apply the natural law in a routine and conventional manner." App. 48a. But even if the point were debatable, it would not diminish the need for this Court's guidance on step one.

The only element that Vanda says was unconventional is "the use of iloperidone to treat schizophrenia." Opp. 9. Yet Vanda never mentions its conces-

sion that "iloperidone was known to treat schizophrenia." C.A. App. 10234. Indeed, Vanda's patent acknowledges that "[i]loperidone and methods for its * * * use as an antipsychotic" were publicly described in its prior-art patent (C.A. App. 38 (1:36–38)), which taught using iloperidone to reduce "symptoms of schizophrenia" (C.A. App. 103 (111:14–17)). Even now, Vanda admits that "patients [were] taking iloperidone" previously "for schizophrenia." Opp. 3–4. Vanda thus claimed neither "a new drug [n]or a new way of using an existing drug." *Mayo*, 566 U.S. at 87.

Vanda makes much of the district court's nonobviousness decision. Opp. 31. But Vanda ignores that this ruling was "based on the revelation of the natural law underpinning the claims, not in any other aspect of the claims." App. 49a–50a n.1 (Prost, C.J., dissenting); see App. 71a–72a; Pet. 37–38. And whether or not the natural law itself was obvious under §101, it must be "treated as though it were a familiar part of the prior art." *Flook*, 437 U.S. at 592.

That principle renders Vanda's purported "discoveries" moot. Opp. 6. "[O]nce nature's secret * * * was discovered, the state of the art made the [claimed method] a simple step." *Funk Bros.*, 333 U.S. at 132.

3. Even if others could "use," "investigate," or "develop" other methods directed to the same natural law, that would not change the result. Opp. 27. That a claim "does not seek to wholly preempt" a natural law does not make it patent-eligible. *Flook*, 437 U.S. at 589–590 (quotation omitted).

Vanda's claims, however, *do* preempt any use of the natural law. Vanda claimed *both* a reduced dosage for the "poor metabolizer[s]" it "discover[ed]" (Opp. 6) *and* the continued treatment of everyone else

with a normal dosage, which all agree "was in the prior art." Opp. 23 n.4. And since only 3–10% of people are "classified as poor metabolizers" (App. 59a), a doctor's treatment will not change at least 90% of the time. Yet simply by "determin[ing] if the patient has a CYP2D6 poor metabolizer genotype" (App. 4a), doctors will inevitably infringe—even if they only give a normal dosage to a patient with a normal genotype.

4. For the same reason, Vanda's claims are unlike hypothetical claims "on the use of a known antiviral drug to treat cancer" or using "Tylenol effectively [to] treat[] pancreatic cancer." Opp. 33–34. Neither example recites a natural law, much less preempts conventional activity based on such a law. They do not recite, for example, determining whether a patient is suffering from pancreatic cancer, and then administering a certain dosage to patients who are, and a conventional dosage to everyone else.

Vanda's claims do essentially that, and thus "tie up the doctor's subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the [claimed] correlations." *Mayo*, 566 U.S. at 86–87. That is quintessential preemption, which "reinforces" that the claims "are not patent eligible." *Id*. at 87.

* * *

Vanda's counsel previously recognized that the decision below is a "landmark decision" with "broad implications." *Supra* n.1. Review is urgently needed to ensure that invalid method-of-treatment patents do not render *Mayo* a dead letter, stifle innovation by constricting the public domain (IP Profs. Br. 13–16), and frustrate the national policy of "speed[ing] the

introduction of low-cost generic drugs to market." *Caraco*, 566 U.S. at 405.

CONCLUSION

For the foregoing reasons, certiorari should be granted.

Respectfully submitted.

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