No. __-____

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 USA, INC., RESPONDENT

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

PETITION FOR A WRIT OF CERTIORARI

TYLER G. JOHANNES
Winston & Strawn LLP
35 West Wacker Drive
Chicago, IL 60601
(312) 558-5600

STEFFEN N. JOHNSON
Counsel of Record
CHARLES B. KLEIN
ANDREW C. NICHOLS
SHARON LIN
Winston & Strawn LLP
1700 K Street N.W.
Washington, DC 20006
(202) 282-5000
sjohnson@winston.com

Counsel for Petitioners

QUESTION PRESENTED

This Court has repeatedly held that "natural phenomena[] and abstract ideas are not patentable" under Section 101 of the Patent Act. *E.g.*, *Alice Corp. Pty. Ltd.* v. *CLS Bank, Int'l*, 573 U.S. 208, 216 (2014). Thus, "a process that focuses upon the use of a natural law" must "also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Mayo Collaborative Servs.* v. *Prometheus Labs., Inc.*, 566 U.S. 66, 72-73 (2012). *Mayo*, for example, invalidated a medical diagnosis method patent that was just "an instruction to doctors to apply the applicable laws when treating their patients." *Id.* at 79.

In the decision below, a divided Federal Circuit panel did exactly what *Mayo* forbids: it exempted all patent claims that are drafted as reciting a method of medically *treating* patients from this analysis. Citing the ruling, the Patent and Trademark Office has directed its examiners that "(1) 'method of treatment' claims that practically apply natural relationships should be considered patent eligible under * * * the USPTO's subject matter eligibility guidance; and (2) it is not necessary for 'method of treatment' claims that practically apply natural relationships to include nonroutine or unconventional steps to be considered patent eligible under [Section 101]."

The question presented is whether patents that claim a method of medically treating a patient automatically satisfy Section 101 of the Patent Act, even if they apply a natural law using only routine and conventional steps.

PARTIES TO THE PROCEEDINGS

Petitioners are Hikma Pharmaceuticals USA Inc. and Hikma Pharmaceuticals International Ltd. (formerly known as West-Ward Pharmaceuticals International Ltd.). Both companies are wholly-owned subsidiaries of Hikma Pharmaceuticals PLC, which is a publicly held corporation traded on the London Stock Exchange under the symbol HIK.L. No other publicly held corporation owns 10% or more of the stock in Hikma Pharmaceuticals USA, Inc. or West-Ward Pharmaceuticals International Limited.

Respondent is Vanda Pharmaceuticals USA, Inc. Aventisub LLC was a plaintiff in the district court.

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Other Authorities

INTRODUCTION

Petitioners ("Hikma") seek review of a divided Federal Circuit decision that purports to render a large category of critical patents—those covering methods of medical treatment—*automatically* eligible for patenting under Section 101 of the Patent Act. Citing this ruling, the Patent and Trademark Office ("PTO") has declared that "it is not necessary for 'method of treatment' claims that practically apply natural relationships to include nonroutine or unconventional steps to be considered patent eligible." That result effectively overrules *Mayo Collaborative Services* v. *Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012)—which held that patents claiming similar methods of medical diagnosis must satisfy ordinary Section 101 analysis—and like decisions holding that all patents are subject to such analysis. As the leading patent law blogger put it, the decision below is a "high flaunting of Supreme Court precedent." Crouch, *Vanda on Rehearing: Will the Federal Circuit Defy SCOTUS?* Patently-O (Jun. 27, 2018).[1]

Section 101 provides that, subject to certain limitations, a patent may be granted to anyone who "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof." 35 U.S.C. § 101. As this Court has repeatedly held, however, "a law of nature cannot be the subject of a patent"—even if that law is newly discovered. *Parker* v. *Flook*, 437 U.S. 584, 589 (1978). Nor can "a process reciting a law of nature, unless that process has additional

---

[1] https://patentlyo.com/patent/2018/06/rehearing-federal-circuit.html.

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.

To be patent-eligible, therefore, an application of a natural law must be "the product of invention," *Funk Brothers Seed Co.* v. *Kalo Inoculant Co.*, 333 U.S. 127, 132 (1948), and the natural law itself must be deemed "part of the prior art," *Flook*, 437 U.S. at 592. If the application is "a simple step" based on "the discovery of the natural principle itself," a claim is not patent-eligible. *Funk Bros.*, 333 U.S. at 132. And "to transform an unpatentable law of nature into a patent-eligible application of such a law, one must do more than simply state the law of nature while adding the words 'apply it.'" *Mayo*, 566 U.S. at 72.

In square conflict with this Court's decisions, the divided ruling below creates a major exception to this settled framework. Under that decision, claims that recite methods of medical treatment—such as administering a known drug for a known purpose—are automatically patent-eligible under Section 101. The patent held by respondent ("Vanda") claims a method of treating schizophrenia patients with the drug iloperidone whereby doctors must adjust the drug's dosage based on the patient's genotype. According to the majority below, such claims fall outside *Mayo*—which invalidated a patent claim that directed doctors to measure the patient's metabolite level and to recognize whether that level "indicate[d] a need" to adjust the drug's dosage. 566 U.S. at 74-75. Why? Purportedly because the claims "recite more than the natural relationship"—"they recite a method of treating patients based on this relationship." App. 35a.

As the dissent forcefully explained, however, that view "does not heed [*Mayo*'s] warning" against "'draft-

ing effort[s] designed to monopolize the law of nature itself." App. 47a (Prost, C.J.). The patent here "simply discloses the natural law that a known side effect of the existing treatment could be reduced by administering a lower dose" to "poor-metabolizers" of the drug. App. 48a. *Mayo* held that "a patent must do more than simply state the law of nature and add the words 'apply it,'" but the claims here "do no more." App. 44a (quoting *Mayo*, 566 U.S. at 72).

As a result, diagnosis claims can now be redrafted as treatment claims that merely direct doctors to follow the natural law in administering known drugs for their known purposes—effectively rendering *Mayo* a dead letter. Further, the ruling below resurrects the rejected idea that "post-solution activity, no matter how conventional," can "transform an unpatentable principle into a patentable process." *Flook*, 437 U.S. at 590. Now, a "competent draftsman [can] attach some form of post-solution activity," such as administering a known drug for a known purpose, "to almost any" natural law—a result that this Court rejected as "exalt[ing] form over substance." *Ibid.*

The Federal Circuit itself has since stated that the decision "underscore[s] the distinction between method of treatment claims and those in *Mayo*." *Roche Molecular Sys., Inc.* v. *CEPHEID*, 905 F.3d 1363, 1373 n.7 (Fed. Cir. 2018). And commentators have noted that the decision "valid[ates] [] the strategy for U.S. patent protection of pursuing claims directed to a method of treatment based on the results of a specific diagnostic test recited in the claims." Miller and Amos, *ARE Patent Law Alert: "Diagnose and Treat" Claims Held Patentable By Federal Circuit—A Path Forward For Patentability*, Amster Rothstein & Ebenstein LLP (Apr. 20, 2018).

If any doubt remained that patentees (and courts) would rely on the ruling below to obtain (and uphold) myriad patents claiming routine applications of natural laws, however, it would be dispelled by the PTO's recent Memo to Examiners concerning the decision:

> (1) "method of treatment" claims that practically apply natural relationships should be considered **patent eligible** under * * * the USPTO's subject matter eligibility guidance; and
>
> (2) it is not necessary for "method of treatment" claims that practically apply natural relationships to include nonroutine or unconventional steps to be considered **patent eligible** under 35 U.S.C. § 101.

Bahr, Memo, *Recent Subject Matter Eligibility Decision: Vanda Pharm. Inc.* v. *West-Ward Pharm.* (Jun. 7, 2018) ("PTO Memo") (App. 98a-99a).[2]

Finally, the need for review is underscored by the fact that "method of use" patents are one of a limited number of patent types that drug makers may list in the Food & Drug Administration's Orange Book.[3] 21 C.F.R. § 314.53(b)(1). Doing so enables these manufacturers to obtain an automatic 30-month stay of generic competition while the parties litigate invalidity and infringement. 21 U.S.C. § 355(j)(5)(B)(iii). The

---

[2] https://www.uspto.gov/sites/default/files/documents/memo-vanda-20180607.PDF.

[3] The Orange Book lists patents that, according to brand-name manufacturers, claim approved drugs or methods of using such drugs. See *Caraco Pharm. Labs., Ltd.* v. *Novo Nordisk A/S*, 566 U.S. 399, 405-406 (2012).

ruling below will heighten patentees' incentive to list weak "method of use" patents in the Orange Book—further delaying low-cost generic medicines' market entry—safe in the knowledge that such patents will now receive a free pass under Section 101.

Certiorari should be granted.

OPINIONS BELOW

The Federal Circuit's opinion (App. 1a-50a) is reported at 887 F.3d 1117. The Federal Circuit's order denying rehearing and rehearing en banc (App. 93a-94a) is unreported. The decision of the District Court for the District of Delaware (Sleet, J.) (App. 51a-92a) is reported at 203 F. Supp. 3d 412.

JURISDICTION

The Federal Circuit properly found jurisdiction because "Vanda's complaint alleged that [Hikma] infringed the '610 patent," which established jurisdiction pursuant to 28 U.S.C. § 1338(a). App. 10a. The court entered judgment on April 13, 2018, and denied a timely rehearing petition on August 14, 2018. On October 31, 2018, the Chief Justice extended the time to petition for certiorari to December 27, 2018. This Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY AND REGULATORY PROVISIONS INVOLVED

Section 101 of the Patent Act provides:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

STATEMENT

A. This Court's longstanding prohibition on patenting natural laws

Section 101 of the Patent Act states the criteria for patent eligibility—the initial hurdle that must be cleared to obtain a patent. "'Laws of nature, natural phenomena, and abstract ideas' are not patentable" under Section 101. *Mayo*, 566 U.S. at 70 (collecting cases). The reason is that these "are the basic tools of scientific and technological work." *Gottschalk* v. *Benson*, 409 U.S. 63, 67 (1972).[4]

The prohibition on patenting natural laws and phenomena goes back more than 150 years. For instance, in *Le Roy* v. *Tatham*, 55 U.S. (14 How.) 156 (1853), this Court recognized that "a new power" cannot be patented, "should one be discovered in addition to those already known." *Id.* at 175. Such powers—whether electricity or a new steam power—are "alike open to all." *Ibid.* The next year, in *O'Reilly* v. *Morse*, 56 U.S. (15 How.) 62 (1854), Samuel Morse claimed "the exclusive right to every improvement where the motive power is the electric or galvanic current, and the result is the marking or printing intelligible characters, signs, or letters at a distance." *Id.* at 112. Morse expressly styled his invention as "a new application of that power." *Ibid.* Yet the Court invalidated his patent, holding that the law required a more specific "mode of applying" a principle. *Id.* at

---

[4] Other requirements for obtaining a patent include novelty (section 102), non-obviousness (section 103), and written description, non-enablement, and definiteness (section 112).

116. And 70 years ago, this Court affirmed that this requirement flows from "the meaning of the patent statutes," namely, the requirement for "an invention or discovery." *Funk Bros.*, 333 U.S. at 132.

B. This Court's recent decisions striking down method patents under Section 101

In keeping with the foregoing precedent, the Court has more recently invalidated several method patents that did not qualify as eligible "inventions" under Section 101, even though they did not claim the natural law itself. The claimed methods were routine, and thus did not display the creativity required to be eligible for a patent.

For instance, in *Flook*, this Court struck down a patent directed to an application of a mathematical formula. The patent, which claimed a "method for updating alarm limits" in catalytic converters and the like, required the user to (i) measure a variable, (ii) use a formula "to calculate an updated alarm-limit value," and (iii) adjust the alarm limit to the updated value. 437 U.S. at 585. As the Court recognized, the asserted claims did not "'wholly preempt the mathematical formula' since there [were] uses of his formula outside the petrochemical and oil-refining industries that remain[ed] in the public domain." *Id.* at 589-590. Nevertheless, the claims were a routine application of the formula; "the use of alarm limits to trigger alarms" and the calculation of alarm limit values were well known. *Id*. at 584.

Two aspects of *Flook*'s Section 101 analysis remain critical today. First, the Court rejected the view that the "adjustment of the alarm limit * * * according to the formula" made the claim patent-eligible because the claim did not merely recite the natural law;

it instructed the user to *do something with* it. *Id.* at 590. As the Court explained, if "post-solution activity, no matter how conventional or obvious in itself," could "transform an unpatentable principle into a patentable process," patent eligibility would "depend simply on the draftsman's art." *Id.* at 590, 593.

Second, the Court reiterated that, to satisfy Section 101, the claimed "process itself, not merely the mathematical algorithm, must be new and useful." *Id.* at 591. In assessing whether the claimed method adds anything significant to the natural law, that law, even if newly discovered, "is treated as though it were a familiar part of the prior art." *Id.* at 592.

Similarly, *Mayo* invalidated a claimed method because it directed the audience to apply a natural law in a routine way. The patent covered the administration of a specific drug (thiopurine), the measurement of a specific metabolite (6-thioguanine), and treatment for a specific type of disease (immune-mediated gastrointestinal disorder). But "doctors used thiopurine drugs to treat patients suffering from autoimmune disorders long before anyone asserted these claims." 566 U.S. at 78. Nevertheless, in a decision authored by Judge Lourie, who also authored the decision below, the Federal Circuit upheld the claims, holding that they were "in effect claims to methods of treatment, which are always transformative when one of a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition." *Prometheus Labs., Inc.* v. *Mayo Collaborative Servs.*, 628 F.3d 1347, 1356 (Fed. Cir. 2010). There too, the Federal Circuit attempted to hold that claims reciting methods of treatment, involving a specific drug, were always patent-eligible.

This Court reversed, holding that the patent "set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." *Mayo*, 566 U.S. at 77. The patented method "simply t[old] doctors to gather data from which they may draw an inference in light of the" natural law; this "amount[ed] to nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients." *Id.* at 79. After all, doctors "routinely measured metabolites as part of their investigations into the relationships between metabolite levels and efficacy and toxicity of thiopurine compounds." *Ibid.* The patent thus merely "append[ed] conventional steps, specified at a high level of generality," to a "law[] of nature." *Id.* at 82.

Most recently, the Court applied this analysis in *Alice Corp. Pty, Ltd.* v. *CLS Bank Int'l*, 573 U.S. 208 (2014). The claims there described a method for mitigating a particular type of financial risk. In reaching its decision, the Court crystallized the two-part inquiry, first set out in *Mayo*, that governs Section 101 analysis:

> First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. * * * If so, we then ask, what else is there in the claims before us? * * * We have described step two of this analysis as a search for an inventive concept—*i.e.*, an element or combination of elements that is sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself.

573 U.S. at 217-218 (internal quotation marks, citations, and brackets omitted). The Court in *Alice* recognized that the challenged claims were directed to an abstract idea, and "if a patent's recitation of a computer amounts to a mere instruction to implement an abstract idea on a computer," such an addition "cannot impart patent eligibility." *Id.* at 223 (internal quotation marks and citations omitted). "Given the ubiquity of computers, * * *, wholly generic computer implementation is not generally the sort of additional feature that provides any practical assurance that the process is more than a drafting effort designed to monopolize the abstract idea itself." *Ibid.* (internal quotations, citation, and brackets omitted).

C. Vanda asserts patent claims that recite a routine application of a natural law.

This case involves the validity of a patent on methods of using the drug iloperidone. In 2013, Hikma gave notice to Vanda that Hikma had filed an Abbreviated New Drug Application (ANDA) with FDA, seeking to market a generic version of Vanda's iloperidone product. App. 62a.

Vanda eventually asserted two patents against Hikma. The '198 patent, which expired in 2016, claimed the iloperidone compound. App. 54a-55a. The '610 patent, which expires in 2027 and is the only remaining patent at issue, claims a method that applies a natural law—the relationship between iloperidone, a particular genotype, and a particular side effect. App. 2a-3a. Claim 1 of the '610 patent, which is representative, reads as follows (CYP2D6 is a particular gene that encodes an enzyme known to metabolize a large number of drugs):

> A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of:
>
> Determining whether the patient is a CYP2D6 poor metabolizer by:
>
> Obtaining or having obtained a biological sample from the patient; and
>
> Performing or having performed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype;
>
> And if the patient has a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less,
>
> And if the patient does not have a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day,
>
> Wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.

App. 3a-4a (paragraph breaks added). The '610 patent thus recites a natural law—"a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal admin-

istration of 12 mg/day or less"—and merely instructs doctors to apply that law to treat their patients.

D. The district court's decision

Following a bench trial, the district court held that the '610 patent claimed eligible subject matter under Section 101. Applying the *Mayo*/*Alice* two-step framework, the court acknowledged that "the asserted claims depend upon laws of nature"—specifically, "on the relationship between iloperidone, CYP2D6 metabolism, and QTc prolongation." App. 76a. The claims were thus invalid unless they "incorporate[d] some additional step sufficient to transform the claims, making them valid." *Ibid.*

Turning to the second step, the court recognized that "it may have been conventional to investigate for side-effects." App. 77a. Nevertheless, the court held that "the precise test and the discovered results" were not routine (*ibid.*)—even though the "discovered results" are nothing more than the natural law itself, which must be treated as prior art. The court then declared that the claimed method applies "only to a specific patient population based upon their genetic composition." App. 78a. That is incorrect: The claimed method directs doctors to apply the law to every patient, with normal metabolizers receiving a higher dose and poor metabolizers receiving a lower dose.

E. The Federal Circuit's decision

A divided panel of the Federal Circuit affirmed. Unlike the district court, however, the panel majority rested its conclusion on *Mayo*/*Alice* step one. In the majority's view, "[t]he inventors [here] recognized the relationships between iloperidone, CYP2D6 metabolism, and QTc prolongation"—i.e., the natural law—

"but that is not what they claimed." App. 32a. Rather, they claimed what the court called "treatment steps"—administering iloperidone to patients. The majority did not explain how these "treatment steps" are anything more than an instruction to apply the natural law in routine fashion.

Chief Judge Prost dissented, finding "no distinction" between this case and *Mayo* and explaining that the majority's decision "depart[ed] from the Supreme Court's holding." App. 47a, 50a. As she recognized, the claimed method is "no more than an optimization of an existing treatment of schizophrenia, just as the claims in *Mayo* concerned 'optimizing therapeutic efficacy' of thiopurine drugs." App. 47a. "The audience of physicians treating schizophrenia with iloperidone long predated the '610 patent." App. 48a. And "reciting specific metes and bounds in the claims did not prevent the Supreme Court from concluding those claims set forth a natural law in *Mayo*." App. 47a.

Chief Judge Prost also recognized that nothing in the claims was an "inventive concept" that could render the claims patent-eligible at *Mayo/Alice* step two. For instance, "the specific dosage adds nothing inventive to the claims beyond the natural law." App. 48a. Nor did the specific "means of identifying a patient's genotype (a 'genetic assay')"; this was "purely conventional pre-solution activity." *Ibid.* Chief Judge Prost also found no meaningful difference between "requiring a dosage," as in these claims, and "indicating a dosage," as in *Mayo*. Neither is an inventive concept.

Chief Judge Prost acknowledged this Court's observation in *Mayo* that the claims there did not "confine their reach to particular applications of [natural]

laws"—and thus were "[u]nlike, say, a typical patent on a new drug or a new way of using an existing drug." App. 49a. But as she explained: "Whatever weight can be ascribed to the foregoing statements about methods of treatment, we remain beholden to the holding of *Mayo*, which, in my view, requires us to find the claims directed to a natural law at step one. (And I find no inventive concept in the claims once the natural law at issue is properly understood in view of *Mayo*.)" *Ibid.* She also reasoned that "[t]he majority does not heed [*Mayo*'s] warning" against "'drafting effort[s] designed to monopolize the law of nature itself.'" App. 47a (quoting 566 U.S. at 77).

Thus, the three opinions below disagree not only about the result, but about nearly every aspect of the analysis. The district court properly held that the claims were directed to a natural law, but nevertheless were valid at *Mayo* step two. The Federal Circuit majority held that the claims were not directed to a natural law, and thus were valid at *Mayo* step one. The dissent properly held that the claims failed both steps. As these disparate approaches confirm, further guidance from this Court is needed.

REASONS FOR GRANTING THE PETITION

The Federal Circuit's divided decision in this case urgently warrants certiorari. Going forward, a large and critical class of patent claims—those that are drafted as reciting methods of medical treatment—will automatically be patent-eligible under Section 101. Citing the ruling, the Patent Office has directed examiners to stop asking whether such claims describe any non-routine or unconventional activity. That result conflicts with the Court's Section 101 precedents, and in particular *Mayo* and *Flook*—which patentees can now circumvent with mere draftsmanship. And the importance of method-of-treatment claims is magnified by the fact that they may be listed in FDA's Orange Book, entitling the patentee to an automatic 30-month stay of FDA approval while the parties litigate invalidity and infringement—delaying generic competition.

This Court's review is urgently needed to protect the integrity of its decisions and to ensure that invalid method-of-treatment patents do not unfairly delay the availability of vital lower-cost generic medicines.

I. The decision below exempts a large and vital class of patents from any search for an "inventive concept" under Section 101, in conflict with *Mayo* and this Court's other Section 101 decisions.

The Federal Circuit's decision breaks sharply from this Court's precedents holding that, to satisfy Section 101, all types of patents directed to natural laws must add some inventive concept beyond routine and conventional scientific acts. The conflict with *Mayo* is especially sharp, as medical diagnosis claims can easily be redrafted as method-of-treatment claims—thus

circumventing Section 101 scrutiny—and the decision below likewise contravenes *Flook*'s teaching that "post-solution activity" cannot render a process eligible for a patent. 437 U.S. at 590. Moreover, given the large number of existing method-of-treatment patents, the decision below holds the potential to deter innovation, and erect an unwarranted barrier to low-cost generic competition, in a critical sector of the economy. Review is warranted.

A. The decision below immunizes method-of treatment-claims from scrutiny under Section 101, even if they recite only routine, conventional activity.

1. Under this Court's longstanding interpretation of the Patent Act, "a law of nature cannot be the subject of a patent." *Flook*, 437 U.S. at 589. Nor can "a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed to monopolize the law of nature itself." *Mayo*, 566 U.S. at 77.

Accordingly, this Court has adopted "a [two-part] framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice*, 573 U.S. at 217 (citing *Mayo*, 566 U.S. at 73). The court must first ask "whether the claims at issue are directed to one of those patent-ineligible concepts." *Ibid.* If so, the court must then "consider the elements of each claim both individually and as an ordered combination to determine whether" the claim contains "additional elements [that] transform the nature of the claim into a patent-eligible application." *Ibid.* (quotations omitted).

The second step is "a search for an 'inventive concept'"—something "significantly more than a patent upon the [ineligible concept] itself" (*id.* at 217-218), and more than "well-understood, routine, conventional activity already engaged in by the scientific community." *Mayo*, 566 U.S. at 79-80. Absent that "something more," the claims lack the inventive creativity needed for patent-eligibility. In conducting this inquiry, moreover, courts must treat any natural law as "part of the prior art." *Flook*, 437 U.S. at 592.

The Court applies this basic Section 101 approach to all patent types, ranging from life sciences to financial services claims. Forty years ago in *Flook*, for example, the Court invalidated a mechanical patent directed to a "method of updating alarm limits" in the "catalytic conversion process[]." 437 U.S. at 585. *Alice*, by contrast, involved "a computer-implemented scheme for mitigating 'settlement risk.'" 573 U.S. at 212. *Bilski* v. *Kappos* presented "a procedure for instructing buyers and sellers how to protect against the risk of price fluctuations in a discrete section of the economy." 561 U.S. 593, 598 (2010). *Myriad Genetics* invalidated claims to "a naturally occurring segment of deoxyribonucleic acid (DNA)." *Ass'n for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 580 (2013). And *Mayo* involved instructions to doctors: "processes that help doctors who use thiopurine drugs to treat patients with autoimmune diseases determine whether a given dosage level is too low or too high." 566 U.S. at 72.

Mayo's discussion of medical diagnosis and treatment claims is particularly relevant here. The Court there held that "relationships between concentrations of certain metabolites in the blood and the likelihood that dosage of a thiopurine drug will prove ineffective

or cause harm" is a law of nature, and that "a patent that simply describes that relation sets forth a natural law." 566 U.S. at 77. Also of note, the Court in *Flook* recognized that routine, conventional "post-solution activity" cannot render a process eligible for a patent, as a "competent draftsman could attach some form of post-solution activity to almost any mathematical formula." 437 U.S. at 590.

2. In conflict with these precedents, the decision below exempts a whole category of patent claims from any search for an "inventive concept" under Section 101—and based on nothing more than routine "post-solution activity." *Ibid.* As commentators and the PTO have noted (see *infra* at 28-32), patents that are drafted as claiming methods of medical *treatment* will now automatically be held patent-eligible. Courts need no longer ask whether such patents recite anything "significantly more than an instruction to doctors to apply the applicable laws when treating their patients." *Mayo*, 566 U.S. at 79. Vanda's patent "simply discloses the natural law that a known side effect of the existing treatment could be reduced by administering a lower dose" to "poor-metabolizers" of iloperidone, while "adding the words 'apply it.'" App. 44a, 48a (quoting *Mayo*, 566 U.S. at 72) (Prost, C.J., dissenting). Thus, as Chief Judge Prost recognized, the court's decision conflicts with "the holding of *Mayo*, which * * * requires us to find the claims directed to a natural law at step one." App. 49a.

Chief Judge Prost was correct. Vanda's claims instruct doctors to observe whether the patient has a certain characteristic: lower-than-normal metabolizing activity in the gene CYP2D6. App. 2a-3a. The claims also set forth a natural law describing the re-

lationship between this characteristic and the risk of negative effects:

> wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day * * *.

App. 4a. Finally, the claims direct doctors to treat the patient with an increased or decreased dose of drug in accordance with the natural law. *Ibid.*

Inexplicably, however, the court below announced that the claims were not "directed to patent-ineligible subject matter." App. 30a. Thus, the court did not even consider whether the claimed treatment step—increasing or decreasing iloperidone's dosage, based on the natural law—was "well-understood, routine, conventional activity already engaged in by the scientific community." *Mayo*, 566 U.S. at 79-80. Put another way, the court did not ask whether the recited "post-solution activity" was "conventional." *Flook*, 437 U.S. at 590. And when the natural law itself is treated as prior art (as it must be), the patent contains nothing more than "an instruction to doctors to apply the applicable laws when treating their patients." *Mayo*, 566 U.S. at 79.

3. The majority's effort to distinguish *Mayo* turns entirely on the presence of the post-solution "treatment" step, and makes the presence of such a step the touchstone going forward:

- "First, the claims in *Mayo* were not directed to a novel method of treating a disease." App. 31a.

- "Unlike the claim at issue in *Mayo*, the claims here require a treating doctor to administer iloperidone" in certain amounts. App. 32a.
- "[T]he claim in *Mayo* did not involve doctors *using* the natural relationship * * * and lessening 'the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.'" App. 33a.
- "These are treatment steps. In contrast, as shown above, the claim in *Mayo* stated that the metabolite level in blood simply 'indicates' a need to increase or decrease dosage, without prescribing a specific dosage regimen or other added steps to take as a result of that indication." *Ibid*.
- The claims "recite more than the natural relationship * * *. Instead, they recite a method of treating patients based on this relationship." App. 35a.

Even the majority's argument that the claims here "do not 'tie up the doctor's subsequent treatment decision,'" like the claims in *Mayo*, turns on the presence of treatment steps. As the majority explained, "[t]he claim in *Mayo* did not go beyond recognizing * * * a need to increase or decrease a dose," but the claims here "recite the steps of carrying out a dosage regimen." App. 33a.

Nothing in the decision below turns on the *particular* method of treatment that is the subject of these claims. The court nowhere suggested that anything in the claims was nonroutine or unconventional. And as Chief Judge Prost noted, "[t]he audience of physicians treating schizophrenia with iloperidone long predated the '610 patent." App. 48a. In fact, the

iloperidone compound was claimed by the *prior art* '198 patent, which expired in 2016. App. 2a, 54a-55a. And the '610 patent itself openly acknowledges that "[i]loperidone and methods for its * * * use as an antipsychotic * * * are described in [the prior art]." 1 C.A. App. 38 ('610 patent col. 1 ll. 36-38).

Nor did the majority below suggest that the "specific dosages" in the claims (App. 32a) added a non-routine step. On the contrary, it recognized that the specific dosages were significant because "certain ranges of administered iloperidone correlate with the risk of QTc prolongation." *Ibid.* That is a statement of the natural law, which (again) must be "treated as * * * prior art." *Flook*, 437 U.S. at 592.

The majority sought to defend its reliance on a talismanic treatment step by pointing out that, in *Mayo*, this Court distinguished the claims there from "a typical patent on a new drug or a new way of using an existing drug," because they did "not confine their reach to particular applications of [natural] laws." App. 32a (quoting *Mayo*, 566 U.S. at 87). Yet the Court was making a narrow point: to the extent that preemption of the use of a natural law is a concern, claims to a "new way of using an existing drug" are narrower than the diagnosis claim in *Mayo*, because they require additional steps. But preemption was not dispositive in *Mayo*; it "simply reinforce[d]" the Court's conclusion and "eliminat[ed] any temptation to depart from case law precedent." 566 U.S. at 87.

Nothing in *Mayo*—or any other decision of this Court—suggests that method-of-treatment claims are categorically patent-eligible under Section 101, regardless of whether they recite routine or conventional activity. Depending on the circumstances, the

use of an old drug for a new *purpose* not found in the prior art, as when an antiviral drug is used to treat cancer, for example, would demonstrate the creativity necessary to satisfy Section 101. But the claims here—administering a prior art drug for a prior art purpose—are utterly conventional.

B. The decision below enables patentees to circumvent *Mayo* and *Flook* by simple draftsmanship.

The Federal Circuit's break from this Court's Section 101 framework would itself warrant certiorari. The importance of that break is magnified, however, by the fact that would-be patentees can now easily circumvent *Mayo*'s holding by employing "'drafting effort[s] designed to monopolize the law of nature itself." App. 47a (Prost, C.J.) (quoting *Mayo*, 566 U.S. at 77). Similarly, a "competent draftsman" can now easily circumvent *Flook* by reciting some "post-solution activity, no matter how conventional," and thus "transform an unpatentable principle into a patentable process." *Flook*, 437 U.S. at 590.

The Federal Circuit has already described the ruling below as "underscor[ing] the distinction between method of treatment claims and those in *Mayo*." *CEPHEID*, 905 F.3d at 1373 n.7. And on account of the Federal Circuit's exclusive appellate jurisdiction over matters "relating to patents" (28 U.S.C. § 1295(a)(1)), the decision below—which every district court, the PTO, and the International Trade Commission must follow—threatens to effectively overrule *Mayo* and *Flook*.[5] As one commentator put it, the de-

[5] District courts and the PTAB have already begun citing the decision below for the rule that "method of treatment

cision below is a "high flaunting of Supreme Court precedent." Crouch, *supra*, at 1. Since no other circuit can address the question presented, only this Court can protect the integrity of its precedents in this context.

1. *Mayo* addressed the patent-eligibility of medical diagnosis claims. The patent there set forth "relationships 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. In addition, the claims told "doctors to gather data from which they may draw an inference in light of the correlations." *Id.* at 79. But as the court below repeatedly emphasized, the claims did not instruct a doctor to administer thiopurine based on such inferences.

Under the decision below, virtually any diagnosis claim—including the claims at issue in *Mayo*—can be redrafted as a treatment claim and avoid Section 101 scrutiny. For instance, rather than merely reciting

---

claims" are not "implicated by * * * *Mayo* and *Myriad*.'" *In re Biogen '755 Patent Litig.*, —F. Supp. 3d— , 2018 WL 4676048, *31 (D.N.J. Sep. 28, 2018); see also *Pernix Ireland Pain DAC* v. *Alvogen Malta Operations Ltd.*, 2018 WL 2225113, *23 (D. Del. May 15, 2018) (Bryson, J., sitting by designation) (upholding claims that were "indistinguishable from the representative claim discussed in" the decision below); *Ex Parte Tim Nielsen & Peter Bornert*, 2018 WL 3830259, *4 (PTAB July 26, 2018) (explaining that the decision below "distinguished claims involving using acquired patient information to modify a drug administration regimen from the claims at issue in *Mayo*, which involved acquiring patient information but did not require any particular use of the acquired information").

that a certain level of metabolite "indicates a need to increase the amount of said drug," the patentee in *Mayo* could have required that the audience actually increase the amount of said drug upon observing a certain level of metabolite. Such a rewritten claim would be no more than "an instruction to doctors to apply the applicable laws when treating their patients." *Mayo*, 566 U.S. at 79. In fact, it is hard to imagine a clearer example of such an "instruction." Based on the decision below, however, such a claim would satisfy Section 101.

Other claims could be redrafted the same way. As *Mayo* indicates, a natural law can be any relationship between two variables, such as patient characteristic, on the one hand, and drug efficacy or toxicity, on the other. The natural law dictates that patients with a particular characteristic respond to the drug one way, while other patients respond differently. This virtually always has ramifications for patient treatment. Under the ruling below, rather than merely set forth the natural law, the patentee can add a conventional treatment step, instructing the doctor to do exactly what the natural law requires, and thereby avoid inquiry into whether there is any "inventive concept."

The decision below thus "make[s] patent eligibility 'depend simply on the draftsman's art.'" *Mayo*, 566 U.S. at 72 (quoting *Flook*, 437 U.S. at 593). By drafting treatment claims, patentees can avoid the issue of whether the claims "do significantly more than simply describe these natural relations." *Id.* at 77.

2. The effects of the decision below will be felt far beyond medical diagnosis claims. *Flook* firmly rejected the "notion that post-solution activity, no matter how conventional or obvious in itself, can transform

an unpatentable principle into a patentable process." 437 U.S. at 590. Why? Because a "competent draftsman could attach some form of post-solution activity to almost any mathematical formula." *Id.* The decision below, however, resurrects the long-discredited idea that "post-solution activity"—such as administering a known drug for a known purpose—can render a claim patent-eligible.

Flook involved a patent that described "a method of updating alarm limits." 437 U.S. at 585. The method had three steps: (i) "measure[] the * * * process variable," (ii) "use[] an algorithm [*i.e.*, a natural law] to calculate an updated alarm-limit value," and (iii) adjust the actual alarm limit to the updated value. *Id.* at 585-586. As this Court recognized, the claimed process "simply provide[d] a new and presumably better method for calculating alarm limit values" based on the natural law. *Id.* at 594-595.

Under the decision below, patents like that rejected in *Flook* are likely to rise from the ashes. There is no meaningful difference between the "adjustment" step in *Flook* and the "treatment" step in a pharmaceutical claim. Both are post-solution activity. Both are routine: the use and recomputation of alarm limit values were known in the art (*ibid.*), as was the administration of iloperidone to treat schizophrenia here (App. 48a (Prost, C.J., dissenting); 1 C.A. App. Vol. 1 38 ('610 patent col. 1 ll. 36-38)). The same is true of the administration of many other drug compounds to treat other diseases. And beyond the pharmaceutical arena, absent this Court's intervention, numerous patents on routine applications of natural laws are sure to issue.

In short, the decision below stands for a simple rule: medical diagnosis claims that recite a "natural relationship" may not be eligible for patent protection, but claims that are drafted to "recite a method of treating patients based on this relationship" are patent-eligible (App. 35a)—*even if* the method "consist[s] of well-understood, routine, conventional activity already engaged in by the scientific community" (*Mayo*, 566 U.S. at 79-80). The decision thus opens the door for all "post-solution activity, no matter how conventional or obvious in itself," to "transform an unpatentable principle into a patentable process." *Flook*, 437 U.S. at 590. This Court should intervene.

C. The decision below allows patentees to impede competition from lower-cost generic drugs and beneficial innovation.

Review is also warranted because, by allowing patent-eligibility to turn on mere draftsmanship, the decision below will result in the issuance of numerous patents that tie up the use of natural phenomena. This will have at least two negative consequences.

First, brand-name drug makers can now protect themselves from competition from lower-cost generic alternatives with patents that violate *Mayo*. The decision will thus frustrate Congress's purpose in enacting the Hatch-Waxman Act, which created a process "designed to speed the introduction of low-cost generic drugs to market." *Caraco*, 566 U.S. at 405.

Brand-name drug manufacturers may list method of treatment patents in the Orange Book, which enables these manufacturers to obtain an automatic 30-month stay of generic competition while the parties litigate invalidity and infringement. 21 U.S.C. § 355(j)(5)(B)(iii). In fact, as of December 2018, the

Orange Book lists 2,379 unique method patents.[6] Accordingly, brand-name manufacturers will be encouraged to apply for and list patents that cover routine applications of their drugs in accordance with natural laws and, under a proper reading of *Mayo*, never should have issued. On account of the automatic 30-month stay, these patents will nevertheless unduly delay the entry of lower-cost generic drugs.

Second, the ruling below powerfully demonstrates how method-of-treatment claims raise the preemption issues discussed in *Mayo*. 566 U.S. at 72. Contrary to the assertion of the majority below (at 32a-33a), the claims here effectively tie up all future use of iloperidone to treat schizophrenia. The relevant natural law governs the relationship between drug dosage and one particular patient characteristic. Thus, doctors will have to consider and apply the natural law recited in Vanda's claims *whenever they administer iloperidone*.

The majority below may have believed that the claims cover only the treatment of poor metabolizers with a lowered dose, but that is not what the claims say. They cover the treatment of *everyone*, with an appropriate dose as determined by the natural law. Accordingly, doctors and researchers will not be able to refine their use of the drug—for example, by discovering *other* characteristics that may affect its efficacy or toxicity, or by refining the dosage regimen. Doctors who developed such refinements would risk inducing infringement, because doctors who applied the refinements would *also* have to consider the nat-

---

[6] https://www.fda.gov/drugs/informationondrugs/ucm129689.htm (Orange Book Data Files) (accessed Dec. 17, 2018).

ural law recited in Vanda's claims. See *Mayo*, 566 U.S. at 86-87 (expressing a similar concern).

II. The Patent and Trademark Office has instructed its Examiners to follow the rule established by the decision below.

The breadth of the Federal Circuit's decision, and the need for review, are underscored by the PTO's actions interpreting that decision. That Office's patent examiners are the gatekeepers of U.S. patent protection, and the Office's directions to them are vitally important. By flagging and interpreting particular court decisions for the examiners, the PTO wields enormous influence over the standards for patentability and, ultimately, what patents issue. And the PTO's reading of the decision below promises method-of-treatment claims a free pass under Section 101, opening the floodgates to such claims.

In June 2018, PTO Deputy Commissioner for Patent Examination Policy, Robert Bahr, issued a memorandum to patent examiners entitled *Recent Subject Matter Eligibility Decision: Vanda Pharmaceuticals Inc.* v. *West-Ward Pharmaceuticals*. The Memo devotes over two pages to "how to evaluate the patent eligibility of 'method of treatment claims' in light of" the decision below—leaving no doubt as to its importance. App. 99a.

After summarizing the decision, which it candidly describes as "illustrat[ing] several important points regarding the subject matter eligibility analysis," the memorandum issues a two-pronged instruction to patent examiners:

> (1) "method of treatment" claims that practically apply natural relationships should be considered **patent eligible** under Step 2A of

> the USPTO's subject matter eligibility guidance; and
>
> (2) it is not necessary for "method of treatment" claims that practically apply natural relationships to include nonroutine or unconventional steps to be considered **patent eligible** under 35 U.S.C. § 101.

App. 97a-99a (paragraph break added). The PTO has thus ensured that all future method-of-treatment patents will issue without undergoing any real scrutiny for an inventive concept. Patentees are now free to claim routine, conventional applications of natural laws, provided those laws are used to treat patients. Certiorari is needed.

III. Commentary on the decision below confirms the importance of granting review.

The importance of the decision below was immediately recognized by the patent bar. Some hailed it as "welcome guidance for pharmaceutical method-of-treatment claims in a post-*Mayo* era,"[7] "good news"

[7] Ratliff II et al., *Federal Circuit Speaks on Patent Eligibility of Method-of-Treatment Claims: Key Takeaways from the Vanda* v. *West-Ward Decision*, Paul Hastings LLP (Apr. 16, 2018), http://www.paulhastings.com/publications-items/details?id=f343866a-2334-6428-811c-ff00004cbded.

for "would-be patentees,"[8] or a "path forward for patentability" of method-of-treatment claims.[9]

Others highlighted the uncertainty created by the decision. For example, noting that "*Vanda* and *Mayo* are very similar," one commentator described the decision as "highlighting the thin—and often unpredictable—line that divides eligible and ineligible subject matter."[10] As he noted, "[t]his decision highlights the difficulty courts have had in applying the Supreme Court's subject-matter eligibility" precedents, and "[g]eneric drug manufacturers must account for this unpredictability in gauging their litigation risks."[11]

More generally, the Federal Circuit has struggled to apply this Court's "directed to" standard. As one commenter noted, "[t]he term is not one that dictionary definitions help with very much," and this "uncertainty allows result-oriented opinions that cannot

---

[8] *Federal Circuit, USPTO Clarify Subject Matter Eligibility for Methods of Treatment*, Foley & Lardner LLP (Jun. 26, 2018), https://www.foley.com/federal-circuit-uspto-clarify-subject-matter-eligibility-for-methods-of-treatment-06-26-2018/.

[9] Miller and Amos, *ARE Patent Law Alert: "Diagnose and Treat" Claims Held Patentable By Federal Circuit—A Path Forward For Patentability*, Amster Rothstein & Ebenstein LLP (Apr. 20, 2018), https://www.arelaw.com/publications/view/alert042018/.

[10] Sivinski, *Vanda* v. *West Ward: This Time, Dosage Adjustment Claims Are Patent-Eligible Subject Matter*, IP-Watchdog (May 16, 2018), https://www.ipwatchdog.com/2018/05/16/vanda-v-west-ward-dosage-adjustment-claims-patent-eligible/id=97117/.

[11] *Ibid.*

readily lead to any meaningful settling of this fundamental issue."[12] This case presents an opportunity for this Court to clarify the concept going forward.

Still others stressed that patentability in this context will now turn on "drafting efforts," as would-be patentees will "increasingly seek to present claims as method-of-treatment claims" (*Vanda*) "rather than methods 'of optimizing therapeutic efficacy for treatment'" (*Mayo*) by "[i]ncluding an affirmative step of administering a drug" or "specific dosages."[13] In the same vein, another writer recognized that, "by adding particularized treatment steps, it may be possible to reclaim patent eligibility for diagnostic claims."[14]

The leading patent law blogger, Professor Dennis Crouch, described the decision as a "high flaunting of Supreme Court precedent." Crouch, *supra*, at 1. As he has explained, "the majority's approach appears to latch onto simple patent drafting tricks as the basis for distinguishing *Mayo*—an approach directly reject-

---

[12] Meyer, *Our Attention Is Now Directed To: "Directed To,"* The Fenwick & West Bilski Blog (Apr. 18, 2018), http://www.bilskiblog.com/blog/2018/04/our-attention-is-now-directed-to-directed-to.html.

[13] Spaith and Morrison, *Federal Circuit Finds Personalized Medicine Invention Subject Matter Eligible*, Dorsey & Whitney LLP (Apr. 17, 2018), https://www.dorsey.com/newsresources/publications/client-alerts/2018/04/federal-circuit-finds-personalized-medicine.

[14] Davison and Tellekson, *A Cautiously Optimistic Diagnosis for Patent Eligibility*, Fenwick & West LLP (May 11, 2018), https://www.fenwick.com/publications/Pages/A-Cautiously-Optimistic-Diagnosis-For-Patent-Eligibility.aspx.

ed by the Supreme Court in *Mayo*."[15] And all seem to agree that "[the decision] is significant because it is the first time the circuit has opined that patent claims that recite a law of nature, but are directed to a method of treating a specific disease based on knowledge of that law of nature, constitutes an application of that law of nature, thereby placing the claim within the scope of patentable subject matter."[16] The widespread commentary on the decision thus confirms the need for review.

IV. This case presents an excellent vehicle for resolving the question presented, and the decision below is incorrect.

This case is also an excellent vehicle to decide the question presented. It squarely presents the question whether treatment claims that direct a doctor to apply a natural law are automatically patent-eligible, regardless of whether they contain any non-routine or unconventional steps. As the PTO has recognized, App. 98a, the Federal Circuit did not consider whether Vanda's claims "add [anything] specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field." *Mayo*, 566 U.S. at 82; see also *supra* at

---

[15] Crouch, *Eligibility: Preamble Does the Trick for Federal Circuit*, PatentlyO (Apr. 15, 2018), https://patentlyo.com/patent/2018/04/eligibility-preamble-federal.html.

[16] Houldsworth, *Federal Circuit upholds Vanda's method-of-treatment claims*, iam (May 7, 2018), https://www.iam-media.com/law-policy/crispr-dust-compulsory-licensing-china-novartis-ceo-wants-us-reform-and-more-aprils (citation omitted).

12-14. Rather, the court held that "the asserted claims are not directed to patent-ineligible subject matter." App. 30a. In justifying this holding, the court established a rule that claims directed to methods of treatment cannot be directed to a natural law.

The resolution of the question presented will control the outcome of this case. If the claims here are subject to the Court's prescribed two-step Section 101 analysis, they are clearly invalid under both steps.

First, at step one, Vanda's claims are plainly directed to a natural law. See *Mayo*, 566 U.S. at 77; *Alice*, 573 U.S. at 217-218. The claims expressly recite that "a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less." App. 4a. That is every bit as much a natural law as are the "relationships between concentrations of certain metabolites" and "the likelihood that a dosage * * * will prove ineffective or cause harm." *Mayo*, 566 U.S. at 77. In both cases, the claims direct the doctor to calibrate dosages for a drug to decrease negative side effects by using a litmus test derived from a natural law—"individualized metabolite" levels in *Mayo*, CYP2D6 genotype here. Even the district court recognized that the claims here could not satisfy the first step of the analysis: they "depend on the relationship between iloperidone, CYP2D6 metabolism, and QTc prolongation." App. 76a.

Second, at step two, the claims add nothing to the natural law other than "well-understood, routine, conventional activity already engaged in by the scientific community." *Mayo*, 566 U.S. at 79-80; see *Alice*, 573 U.S. at 217-218 ("a search for an 'inventive concept'"). As Chief Judge Prost's dissent recognized,

there is "no inventive concept in the claims once the natural law at issue is properly understood." App. 49a. The patent simply claims the application of an ineligible natural law in a particular context. The only scientific advance here is the discovery of the natural law itself. The majority below did not suggest otherwise, and Chief Judge Prost expressly concluded that neither the "specific dosage" step nor the specific "means of identifying a patient's genotype" added anything "inventive to the claims beyond the natural law." App. 48a (dissenting op.).

To see this, it is helpful to examine the claims piece by piece. As the following chart demonstrates, the claims here consist of essentially three parts: a "determining" step, a "wherein" clause and a "treatment" step, albeit in a different order than in *Mayo*.

Mayo	***Vanda***
A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:	A method for treating a patient with iloperidone, wherein the patient is suffering from schizophrenia, the method comprising the steps of:
(a) Administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder;	
(b) Determining the level of 6-thioguanine or 6-methylmercaptopurine in said subject having said immune-mediated gastrointestinal disorder;	Determining whether the patient is a CYP2D6 poor metabolizer by: Obtaining or having obtained a biological sample from the patient; and Performing or having per-

	formed a genotyping assay on the biological sample to determine if the patient has a CYP2D6 poor metabolizer genotype;
	And if the patient has a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount of 12 mg/day or less, and if the patient does not have a CYP2D6 poor metabolizer genotype, then internally administering iloperidone to the patient in an amount that is greater than 12 mg/day, up to 24 mg/day,
Wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and Wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells or a level of 6-methylmercaptopurine greater than about 7000 pmol per $8x10^{over\ 3}$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.	Wherein a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype is lower following the internal administration of 12 mg/day or less than it would be if the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day.

First, as in *Mayo*, the "determining" step is conventional. As the dissent below recognized, just as "methods for determining metabolite levels were well known in the art" (*Mayo*, 566 U.S. at 79), so was the "genotyping assay" required by the claims (App. 48a). As the '610 patent itself states: "Detection means suitable for use in the methods and devices of the present invention include those known in the art." 1 C.A. App. 43 ('610 patent at col. 12 ll. 21-33); *id.* at col. 12 ll. 65-66 ("Detection methods, means, and kits suitable for use in the present invention are described in" the prior art).

Second, as in *Mayo*, the "'wherein' clause[] simply tell[s] a doctor about the relevant natural laws." 566 U.S. at 78. The clause states that "a risk of QTc prolongation for a patient having a CYP2D6 poor metabolizer genotype *is lower* following the internal administration of 12 mg/day or less *than it would be would be if* the iloperidone were administered in an amount of greater than 12 mg/day, up to 24 mg/day." App. 4a (emphasis added). This informs the doctor how to minimize the risk of QTc prolongation.

Third, the treatment step adds nothing creative to the claims. "[D]octors used [iloperidone] drugs to treat patients suffering from [schizophrenia] long before anyone asserted these claims." *Mayo*, 566 U.S. at 78; App. 48a (Prost, C.J., dissenting). Here too, we know this from the '610 patent, which says: "Iloperidone and methods for its * * * use as an antipsychotic * * * are described in" the prior art, and "[i]loperidone can be formulated into dosage units and administered to patients using techniques known in the art." 1 C.A. App. 38 (col. 1 ll. 36-38), 43 (col. 11 ll. 63-64). Thus, both the patent and the prior art involve administering iloperidone to treat schizophrenia.

Even if the specific dosage regimen claimed for poor metabolizers can be said to be new, that is not enough. A method "must be more than new and useful to be patented; it must also satisfy the requirements of invention or discovery." *Funk Brothers*, 333 U.S. at 131. And this Court has firmly rejected the notion that "post-solution activity, no matter how conventional or obvious in itself, can transform an unpatentable principle into a patentable process." *Flook*, 437 U.S. at 590. Rather, the new process must contain "an "inventive concept'—i.e., an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the ineligible concept itself.'" *Alice*, 573 U.S. at 217-18 (quoting *Mayo*, 566 U.S. at 72-73). Here, the administration of a known drug for a known use displays no inventive concept.

The only scientific advance in these claims is the discovery of the natural law itself. The "treatment" step follows directly from that law. Indeed, as Chief Judge Prost recognized, "the district court found nonobviousness based on the revelation of the natural law underpinning the claims, not in any other aspect of the claims." App. 49a-50a n.1 (dissenting op.); 71a ("Plaintiffs argue that it is often the case that no dosage adjustment is needed for CYP2D6 poor metabolizers."); 72a (relying on the "level of clinical testing required and the inherent unpredictability in this field"); *ibid.* ("[e]ven if [the prior art] provided a basis for a POSA [person of ordinary skill in the art] to focus a study on the implications for iloperidone metabolism of mutations in the genes for the CYP2D6, it would have been impossible to predict the results."). But "once nature's secret of the [natural law] was discovered, the state of the art made the [claimed method] a simple step." *Funk Bros.*, 333 U.S. at 132. For

purposes of section 101, "the novelty of the [natural law] is not a determining factor at all." *Flook*, 437 U.S. at 591. Accordingly, the claimed treatment regimen is not an eligible "invention or discovery within the meaning of the patent statutes." *Funk Bros.*, 333 U.S. at 132.

In the end, the asserted claims here are just like those in *Mayo*: "instruction[s] to doctors to apply the applicable laws when treating their patients." 566 U.S. at 79. The claims are thus ineligible for patent protection under Section 101, and are invalid. This Court should grant certiorari to ensure that simple "drafting effort[s]" do not allow drug manufacturers to "monopolize the law[s] of nature," in conflict with this Court's precedents. *Mayo*, 566 U.S. at 77.

CONCLUSION

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

Respectfully submitted.

TYLER G. JOHANNES
Winston & Strawn LLP
35 West Wacker Drive
Chicago, IL 60601
(312) 558-5600

STEFFEN N. JOHNSON
Counsel of Record
CHARLES B. KLEIN
ANDREW C. NICHOLS
SHARON LIN
Winston & Strawn LLP
1700 K Street N.W.
Washington, DC 20006
(202) 282-5000
sjohnson@winston.com

Counsel for Petitioners

DECEMBER 2018