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

BRIEF FOR THE ASSOCIATION FOR ACCESSIBLE MEDICINES AND CERTAIN INDIVIDUAL COMPANIES AS *AMICI CURIAE* IN SUPPORT OF THE PETITION

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INTERESTS OF *AMICI CURIAE*[1]

Amicus Curiae, 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 that are substantially more affordable.

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.

AAM's members are frequently involved in pharmaceutical litigation in which they rely on invalidity defenses such as Section 101 patent eligibility. Invalid patents undermine the legitimacy of the patent system, stifle competition, and impede access to low-cost medicines. Accordingly, AAM members have significant interest in

1. Pursuant to Rule 37.6, *amici* state that no counsel for any party authored this brief in whole or in part, and no person other than *amici* or its counsel have made any monetary contribution intended to fund the preparation or submission of this brief. All parties to this case received timely notice under Rule 37.2(a) of *amici*'s intent to file this brief, and all parties consented to the filing of this brief.

ensuring that brand companies enforce drug monopolies only on patent-eligible claims.

Amici Curiae, Inventia Healthcare Limited ("Inventia") and Mylan Pharmaceuticals, Inc., ("Mylan") have a direct interest in the present petition because of a current lawsuit in the District of Delaware, which involves the same patent-at-issue—U.S. Patent 8,586,610 ("the '610 patent"). *See Vanda Pharms. Inc., v. Inventia Healthcare Ltd.*, C.A. No. 15-362 (D. Del.). Inventia, the named defendant, is the manufacturer of the drug in question, iloperidone, and Mylan has contracted with Inventia to market the drug. The lawsuit is stayed pending the outcome of Hikma's petition for writ of *certiorari*. Because subject matter eligibility is a threshold inquiry, this Court's decision on the patent eligibility of the '610 patent will undoubtedly have direct implications on the case below. *See Parker v. Flook*, 437 U.S. 584, 593 (1978) ("The obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious.").

SUMMARY OF THE ARGUMENT

Hikma's petition for *certiorari* addresses a matter of national importance warranting review. The Court's unanimous decision in *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 566 U.S. 66 (2012) set forth the requirements for patent eligibility under 35 U.S.C § 101 of the Patent Act and invalidated a claimed method because it directed the audience to apply a natural law in a routine way. The decision below has been widely understood to carve out a whole category of method of treatment patents and declared them not subject to those requirements. The

question presented is thus whether patents that claim a method of medically treating a patient automatically satisfy Section 101, even if they apply a natural law using routine and conventional steps. *Amici* respectfully argue that the decision below directly conflicts with *Mayo* and warrants review due to the large number of pharmaceuticals and other products affected by the ruling.

Denial of the petition would lead to untold numbers of future patents improperly issued and existing patents improperly enforced. The Patent and Trademark Office (PTO) has embraced the Federal Circuit's divided opinion below as giving it license to adopt a position that this Court rejected in *Mayo*. As explained in this brief, there is no difference, for purposes of Section 101, between the method of treatment claims upheld in the decision below and the claims struck down by this Court in *Mayo*. The claims in both cases combined a natural law with the same two method steps previously used by those in the field. And the result in both cases was an unpatentable claim directed to a law of nature because a patient's body determined if infringement occurred.

The widely felt urgency for this Court to clarify the implications of *Mayo* for existing as well as future patents was acknowledged earlier this month by the PTO: "[m]any stakeholders, judges, inventors, and practitioners across the spectrum have argued that *something needs to be done* to increase clarity and consistency in how Section 101 is currently applied." *See* 2019 Revised Patent Subject Matter Eligibility Guidance, 84 Fed. Reg. 50 (Jan. 7, 2019) (emphasis added) ("2019 PTO Guidance") (App. 2a).

We respectfully submit that what "needs to be done to increase clarity and consistency in how Section 101 is currently applied" is to grant Hikma's petition. *Id.* If the categorical exception to *Mayo* stands, Section 101 eligibility for future patents will depend on the draftsman's art of camouflaging patent-ineligible claims as treatment steps. Allowing such a practice will also have the immediate consequence of improperly extending the monopoly period of brand name drugs, and wrongly depriving the public of the generic version of a medicine—eleven more years in the case of iloperidone—thus forcing taxpayers and patients to pay monopoly prices of pharmaceuticals for far longer than the patent system should allow under this Court's holding in *Mayo*.

This case illustrates the real world implications when confusion about patent eligibility reigns. This Court can and should dispel the confusion. Hikma's petition for *certiorari* should be granted.

ARGUMENT

I. The Conflict Between *Mayo* and the Decision Below Warrants Resolution by this Court

A. The Decision Below Undermines Competition by Thwarting the Congressional Purpose of the Hatch-Waxman Act

The purpose of the Drug Price Competition and Patent Term Restoration Act of 1984,[2] commonly known as the Hatch-Waxman Act, was to "speed[ ] the introduction of low-cost generic drugs to market thereby furthering

2. Pub. L. No. 98-417, 98 Stat. 1585.

drug competition." *See e.g., F.T.C. v. Actavis, Inc.*, 570 U.S. 136, 142 (2013) (internal citation omitted).[3] Thwarting that statutory purpose, brand companies continue to abuse the patent system to enforce monopolies on brand drugs in a practice known as "evergreening"—filing patents on methods of using the same drug and thereby delaying generic access.[4]

This is a textbook case. Vanda's patent on the iloperidone compound—U.S. Reissue Patent 39,198—expired on November 15, 2016. Petition Appendix ("Pet. App.") 2a. The Federal Circuit's conclusion that *Mayo* does not apply to the '610 patent because it claims a method of treatment allows Vanda to thwart the Congressional purpose for almost *eleven more years* (until November 2, 2027).

Method of treatment patent claims, like the '610 patent, are common fare for pharmaceutical patents. Underscoring the high frequency of these patents is the

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3. *See also Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405 (2012); *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 676 (1990).

4. *See Caraco Pharm. Labs* at 405:

> Because the FDA cannot authorize a generic drug that would infringe a patent, the timing of an ANDA's approval depends on the scope and duration of the patents covering the brand-name drug. Those patents come in different varieties. One type protects the drug compound itself. Another kind—the one at issue here—gives the brand manufacturer exclusive rights over a particular method of using the drug. In some circumstances, a brand manufacturer may hold such a method-of-use patent even after its patent on the drug compound has expired.

fact that 2,379 unique method patents are listed in the Orange Book. *See* Petition at 26-27. Each listed method patent can enable a brand name drug manufacturer to obtain a 30-month automatic stay of generic competition when in litigation. Yet, as this brief later explains, there is no practical distinction for Section 101 purposes between the claims addressed in *Mayo* and the method of treatment claims presented here. These patents serve to take away generic drug treatments that, under *Mayo*, rightfully belong to the public.

If this Court remains silent, the PTO can be expected to issue, and the lower courts enforce, an untold number of improper patents because they are denominated "method of treatment" patents. And indeed, the PTO has already issued guidance to examiners based on this case asserting that "method of treatment claims (which *apply* natural relationships as opposed to being 'directed to' them) were identified by the Supreme Court as *not* being implicated by its decisions in *Mayo* and *Myriad* . . . ." *See* Robert H. Bahr, Memo, *Recent Subject Matter Eligibility Decision: Vanda Pharm. Inc. v. West-Ward Pharm.* (June 7, 2018) (emphasis is that of the PTO) (Pet. App. 98a) ("2018 PTO Memo"). Such a broad categorical exemption from Section 101 for method of treatment patents urgently warrants review.

B. Several Federal Circuit Judges Have Expressed the Need for Clarification of *Mayo*

On the issue of Section 101, Federal Circuit judges have repeatedly requested guidance from this Court. Judge Dyk wrote in *Ariosa*, "further illumination as to the scope of *Mayo* would be beneficial . . . and any

further guidance must come from the Supreme Court, not this court." *See Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 809 F.3d 1282, 1287 (Fed. Cir. 2015) (concurring in denial of rehearing *en banc*). Judge Stoll recently stated at an American Intellectual Property Law Association meeting, "'one of the more challenging issues I've seen since I've been at the court is the 101 test and the *Alice/Mayo* test. . . to the extent there is any need for change that would be for Congress or the Supreme Court.'" *See* Quinn, *Judge Stoll tells AIPLA Alice/Mayo 'a difficult line of cases to administer'*, IPWatchdog (Oct. 26, 2018)[5]; *see also Berkheimer v. HP Inc.*, 890 F.3d 1369, 1375 (Fed. Cir. 2018) (Lourie, J., joined by Newman, J., concurring in denial of rehearing *en banc*) ("Section 101 issues certainly require attention beyond the power of this court.").

The author of the decision below has been critical of *Mayo*.[6] The decision below circumvents *Mayo* by seizing upon isolated statements in the *Mayo* opinion to support

5. http://www.ipwatchdog.com/2018/10/26/judge-stoll-aipla-alice-mayo/id=102708/.

6. *See Berkheimer* at 1375 (Fed. Cir. 2018) (Lourie, J., joined by Newman, J., concurring in denial of rehearing *en banc*):

> The Supreme Court whittled away at the § 101 statute in Mayo by analyzing abstract ideas and natural phenomena with a two-step test, including looking for an "inventive concept" at step two, thereby bringing aspects of §§ 102 and 103 into the eligibility analysis….We now are interpreting what began, when it rarely arose, as a simple § 101 analysis, as a complicated multiple-step consideration of inventiveness ("something more"), with the result that an increasing amount of inventive research is no longer subject to patent.

its conclusion that Vanda's method of treatment claims are not directed to a natural law. *See* Petition at 19-22. The dissenting judge saw clearly that the net effect of the opinion was a decision contrary to the holding in *Mayo*: "[w]hatever 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." Pet. App. 49a; *see also* Petition at 19-22.[7]

II. The Decision Below Allows the PTO to Re-Adopt the Approach to Section 101 that this Court Rejected in *Mayo*

Underscoring the national importance of this decision, the PTO issued two new guidances on Section 101 after the Federal Circuit issued its opinion. In these guidances,

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7. *See also* Pet. App. 47a-48a, (Prost., C. J., dissenting) (internal citations omitted):

> The Court in *Mayo* found that the claim limitation concerning "administering" a thiopurine drug to a patient "simply refer[red] to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs"—an audience that existed long before the patent disclosure. So too here. The audience of physicians treating schizophrenia with iloperidone long predated the '610 patent. The patent simply discloses the natural law that a known side effect of the existing treatment could be reduced by administering a lower dose to CYP2D6 poor-metabolizers. It claims no more than instructions directing that audience to apply the natural law in a routine and conventional manner. The majority fails to reconcile this substantive similarity between our case and *Mayo*.

which specifically discuss this case, the PTO interpreted the divided decision below to effectively carve out method of treatment claims from Section 101: "[t]he *Mayo* claims were not 'method of treatment' claims that practically apply a natural relationship." 2018 PTO Memo (Pet. App. 98a). After Hikma submitted the petition for *certiorari*, the PTO reaffirmed, in the 2019 PTO Guidance, its understanding of the decision below, which established a framework that goes beyond method of treatment claims: "[o]nly when a claim recites a judicial exception and fails to integrate the exception into a practical application, is the claim 'directed to' a judicial exception, thereby triggering the need for further analysis pursuant to the second step of the *Alice/Mayo* test …." App. 4a.[8]

Fairly read, however, this Court's precedent does *not* stand for the proposition that claims which are a "practical application" of a natural relationship necessarily satisfy Section 101, particularly where the steps are routine and conventional. Instead, this Court's pre-*Mayo* precedent held exactly the opposite. *See Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U. S. 127, 131 (1948) (holding a practical application of a law of nature invalid under Section 101) ("The aggregation of select strains of the several species

8. In the 2019 PTO Guidance, the PTO explicitly characterized the decision below as a "practical application." *See* App. 5a:

> *See also Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1135 (Fed. Cir. 2018) (holding claims to the practical application of the natural relationships between iloperidone, CYP2D6 metabolism, and QTc prolongation to treat schizophrenia, not merely the recognition of those relationships, to be patent eligible at Mayo/Alice step 1 (USPTO Step 2A)), and USPTO Vanda Memorandum (discussing *Vanda*).

into one product is an application of that newly-discovered natural principle. But however ingenious the discovery of that natural principle may have been, the application of it is hardly more than an advance in the packaging of the inoculants.").

As the unanimous nature of the *Mayo* opinion suggests, *Mayo* is not an aberration in this Court's jurisprudence. Rather *Mayo* is wholly consistent with *Funk*. Both cases instruct that merely combining conventional activity with a newly discovered natural law is not patent eligible under Section 101.

In its *amicus* brief to this Court in *Mayo*, the Government made the argument, with the PTO as a signatory, that the *administering* and *determining* steps recited in the *Mayo* claims constituted a practical application of a law of nature that made the claimed invention patent eligible. *See* Brief for the United States as *Amicus Curiae* ("Those steps describe a patent-eligible process under Section 101. The claim recites a series of acts in the physical world that achieve a useful end (treatment of auto-immune disorders) by transforming the body chemistry of the patient.").[9]

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9. Brief for the United States as *Amicus Curiae* Supporting Neither Party at pg. 14, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012) (No. 10-1150), 2011 WL 4040414.

The complete quote is as follows:

> Claim 1 of the '623 patent recites a method comprising two affirmative steps: (1) "*administering* a drug providing 6-thioguanine to a subject," and (2) "*determining* the level of 6-thioguanine in said subject." Those steps describe a patent-eligible

Importantly, that argument—which so closely parallels the PTO's new guidance—was unanimously rejected in *Mayo*:

> The Government argues 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 sufficient to satisfy § 101's demands . . . This approach, however, would make the "law of nature" exception to § 101 patentability a dead letter. The approach is therefore not consistent with prior law.

Mayo, 566 U. S. at 89.[10]

Also importantly, the claim at issue in this case, and the claim in *Mayo*, recited the same method steps: a *determining* step and an *administering* step. The steps

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> process under Section 101. The claim recites a series of acts in the physical world that achieve a useful end (treatment of auto-immune disorders) by transforming the body chemistry of the patient.

10. *M*ayo, 566 U.S. at 89, omitted portion of the quote is as follows:

> The Government does not necessarily believe that claims that (like the claims before us) extend just minimally beyond a law of nature should receive patents. But in its view, other statutory provisions—those that insist that a claimed process be novel, 35 U.S.C. § 102, that it not be "obvious in light of prior art," § 103, and that it be "full[y], clear[ly], concise[ly], and exact[ly]" described, § 112—can perform this screening function. In particular, it argues that these claims likely fail for lack of novelty under § 102.

in the claims are reversed (in this case, *determining* comes before *administering*, while in *Mayo* the order is reversed), but in both claims the natural law is applied by the same two steps. *See* Petition at 34-35.

With this background, the method of treatment claims here are revealed to be analytically indistinguishable from the claims in *Mayo*. Inasmuch as a claim reciting the steps of *administering* a drug and *determining* the metabolic result is (per *Mayo*) directed to a law of nature, so too is a claim that recites the steps of first *determining* the metabolism and then *administering* the drug. There is no reasoned basis for finding that one is directed to a natural law and the other not.

The decision below has thus led to the incongruous categorical rule that a "practical application" of a natural law satisfies Section 101 regardless of whether the steps are routine and conventional. Without review from this Court, this broad exemption from *Mayo* for "practical applications" of a natural law can be expected to produce a flood of improperly issued and enforced patents—all the while keeping the public from generic versions of these drugs.

III. For Section 101 Purposes, the Method of Treatment Claims Here and the Claims Unanimously Struck Down in *Mayo* are the Same

A. As in *Mayo*, the Claims Here Seek to Monopolize a Law of Nature by Reciting Conventional Activity

The similarities between the patent at issue here and the patent at issue in *Mayo* help remove the shroud

of skillful patent drafting from an attempt to monopolize the operation of a law of nature. As *Mayo* noted, this Court's precedent "warn[s] us against interpreting patent statutes in ways that make patent eligibility 'depend simply on the draftsman's art' without reference to the 'principles underlying the prohibition against patents for [natural laws].'" *Mayo*, 566 U.S. at 72 (citing *Parker v. Flook*, 437 U.S. 584, 593 (1978)). One of those principles is that inventiveness must be examined apart from the law of nature. *See Flook*, 437 U.S. at 594 ("Even though a phenomenon of nature or mathematical formula may be well known, an inventive application of the principle may be patented. Conversely, the discovery of such a phenomenon cannot support a patent *unless there is some other inventive concept in its application*.") (emphasis added).

The putative invention of the Vanda patent concerns adjusting the dose of the antipsychotic drug, iloperidone, based on a patient's naturally occurring genetic makeup.[11] For a method of treatment using iloperidone to be patent eligible, the method steps must, according to *Flook*, add some inventive concept separate and apart from the natural law. Here there is no such inventive concept for

11. *See* C.A. App. 38, the '610 patent, col. 1, ll. 53-61:

> Mutations in the CYP2D6 gene have been associated with a number of drug metabolism-related phenotypes. These include the ultra rapid metabolizer (UM), extensive metabolizer (EM), intermediate metabolizer (IM), and poor metabolizer (PM) phenotypes. Where a particular drug is capable of producing unwanted physiological effects in its metabolized or non-metabolized forms, it is desirable to determine whether a patient is a poor metabolizer of the drug prior to its administration.

at least two reasons. First, it is the same pair of method steps (*determining* and *administering*) involved here as in *Mayo*, and this Court concluded in *Mayo* that "the steps add nothing of significance to the natural laws themselves."[12] *Id.* at 87. Second, as discussed below, the patentee here admitted these steps were conventional activity.

Genotype testing, and the specific dosages recited in the claims of the '610 patent, were conventional activity previously engaged in by those in the field. *See* Pet. App. 47a (C. J. Prost, dissenting) (concluding both the genotyping and specific dosages add nothing inventive). *See also* 2018 PTO Memo, Pet. App. 97a, where the PTO referred to "the arguably conventional genotyping and treatment steps." In fact, the body of the '610 patent describes that its genotyping testing merely employed commercially available kits used according to the manufacturer's instructions.[13] C.A. App. 40. Similarly,

12. *Mayo*, 566 U.S. at 87:

> We need not, and do not, now decide whether were the steps at issue here less conventional, these features of the claims would prove sufficient to invalidate them. For here, as we have said, the steps add nothing of significance to the natural laws themselves. Unlike, say, a typical patent on a new drug or a new way of using an existing drug, the patent claims do not confine their reach to particular applications of those laws.

13. *See* C.A. App. 40, the '610 Patent, col. 5-6, ll. 56-3:

> Amplification was performed on 40-100 ng of genomic DNA using a GC-rich PCR kit (Roche Diagnostics, Mannheim, Germany) according to the manufacturer's recommendations.

during prosecution of the '610 patent at the PTO, Vanda admitted that a key prior art reference, *Jain*, described the claimed dosages.[14]

B. In Both *Mayo* and the Decision Below, a Law of Nature Determined Whether the Claim is Infringed

This Court has long instructed that Section 101 protects against efforts to monopolize the operation of a law of nature, because a natural law belongs to all. *See e.g., Funk* at 130 (1948) citing *Le Roy v. Tatham*, 55 U.S. (14 How.) 156 (1853).[15] This case involves such an attempt

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* * *

> Third Wave Technologies, Inc (Madison, Wis.) developed the probe sets for genotyping. Genotyping was performed on PCR products using the Invader® assay (Lyamichev 1999) (Third Wave Technologies, Inc) according to the manufacturer's recommendations.

14. *See* Curt D. Wolfgang, *et. al*, United States Patent and Trademark Office Amendment to Non-Final Rejection, Method for Administration of Iloperidone, Application 11/576,178 (March 20, 2013) (App. 6a-8a), where the patentee, Vanda, quoted without disagreement the PTO's characterization of *Jain* (App. 7a):

> Jain provides an overview of several studies of iloperidone, teaching that daily dosages of iloperidone up to 24 mg/day have been 'found to be well tolerated'…. Jain also discloses a long term study of dosages of 4 -16 mg/day (citation omitted), as well as the finding of efficacy at dosages of 8 mg/day….

15. *Funk* at 130 (1948) (internal citation omitted):

> The qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part

to monopolize a law of nature that is at least as blatant as *Mayo*. Accordingly, if the decision below is not reviewed, *Mayo* itself is undermined.

In *Mayo*, infringement depended upon how the patient's body metabolized a given dose of a drug. If the drug dosage produced a level of the metabolite (6-thioguanine) less than 230 pmol, or more than 400 pmol, then the doctor infringed. However, if the 6-thioguanine level was between 230 and 400 pmol, there was no infringement. The same action by the doctor thus infringed, or did not infringe, depending upon how the body metabolized the drug.[16]

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of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes.

16. *Mayo* representative claim 1 (Pet. App. 44a-45a):

A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

(a) administering a drug providing 6–thioguanine to a subject having said immune-mediated gastrointestinal disorder; and

(b) determining the level of 6–thioguanine in said subject having said immune-mediated gastrointestinal disorder,

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

The representative claim at issue in the present case has a similar defect. The district court found one instance of infringement, citing the trial testimony of plaintiff's expert Dr. Gus Alva about his Patient No. 1.[17] Here is the pertinent excerpt of the trial testimony cited by the district court:

> Q. This patient had a genotyping test in 2013 and was an extensive metabolizer. Correct?
>
> A. Correct.
>
> Q. And then we had one treatment in 2013 that was 12 milligrams per day. Correct?
>
> A. Yes.
>
> Q. And two treatments in 2014 that were 12 milligrams per day. Correct?
>
> A. Yes.
>
> Q. And two treatments in 2015 that were 12 milligrams per day. Correct?
>
> A. Yes.

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wherein the level of 6–thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

17. Pet. App. 86a.

> Q. And then one treatment in 2015 that was 16 milligrams a day and one that was 20 milligrams per day. Correct?
>
> A. Correct.

C.A. App. 6999.

Dr. Alva would have been infringing the '610 patent from 2013-2015 if Patient 1 had been a CYP2D6 poor metabolizer, because giving 12 mg/day to a poor metabolizer is an infringement.[18] The administration of

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18. *See* Claim 1 of the '610 patent (Pet. App. 46a) (emphasis added):

> 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*,

12 mg/day for those two years was not an infringement, however, because Patient No. 1's genetic makeup was not that of a poor metabolizer.

Similarly, Dr. Alva became an infringer in 2015 when he increased the dosage to 16 mg/day. The administration of 16 mg/day became an act of infringement because Patient No. 1 "does not have a CYP2D6 poor metabolizer genotype" (quoting claim 1 of the '610 patent). Thus, as in *Mayo*, how the patient metabolized the drug determined whether the drug was being used in an infringing manner.

As noted in the prior section, there is no genuine dispute that the iloperidone doses used by Dr. Alva—the "non-infringing" 12 mg dose and the "infringing" 16 mg dose—were both in the prior art. When this conventional activity is removed from the claim, all that remains is a naked attempt to monopolize the operation of a law of nature. This is because whether conventional activity infringes, or does not infringe, depends upon how the body metabolizes iloperidone.

Just as in *Mayo*, such a claim is directed to a natural law because a patient's body determines if infringement occurs. The claim here does not recite "a *new* way of using an existing drug," *Mayo* at 87 (emphasis added). Rather it recites an old way of using an existing drug that may have benefits depending upon the workings of a newly-

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> 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.

discovered natural principle. Unless *Mayo* is to be honored only in the breach rather than in the observance, review should be granted of the decision below.

CONCLUSION

The decision below has created confusion in the law that threatens harm to the public. In concluding that Vanda's method of treatment claims are not directed to a law of nature, the majority opinion opened the door for a rule which effectively exempts a "practical application" of a natural law from Section 101. This Court's precedent, however, is contrary to such a rule. Allowing the decision below to stand will improperly extend the monopoly period of brand name drugs, and wrongly deprive the public of generic medicines.

Before the decision below does more damage, both to the coherency of the law and to the public interest in affordable medicines, Hikma's petition for *certiorari* should be granted.

Respectfully submitted,

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January 28, 2019

APPENDIX

APPENDIX A — 2019 REVISED PATENT SUBJECT MATTER ELIBILITY GUIDANCE FOR THE UNITED STATES PATENT AND TRADEMARK OFFICE

DEPARTMENT OF COMMERCE

UNITED STATES PATENT AND TRADEMARK OFFICE

Docket No. PTO-P-2018-0053

2019 REVISED PATENT SUBJECT MATTER ELIGIBILITY GUIDANCE

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Patent subject matter eligibility under 35 U.S.C. 101 has been the subject of much attention over the past decade. Recently, much of that attention has focused on how to apply the U.S. Supreme Court's framework for evaluating eligibility (often called the *Alice/Mayo* test).[1] Properly applying the *Alice/Mayo* test in a consistent manner has proven to be difficult, and has caused uncertainty in this area of the law. Among other things, it has become difficult in some cases for inventors, businesses, and other patent stakeholders to reliably and predictably determine what subject matter is patent-eligible. The legal uncertainty surrounding Section 101 poses unique challenges for the USPTO, which must ensure that its more than 8500 patent

1. *Alice Corp. Pty. Ltd.* v. *CLS Bank Int'l,* 573 U.S. 208, 217-18 (2014) (citing *Mayo Collaborative Servs.* v. *Prometheus Labs., Inc.,* 566 U.S. 66 (2012)).

examiners and administrative patent judges apply the *Alice/Mayo* test in a manner that produces reasonably consistent and predictable results across applications, art units and technology fields.

Since the *Alice/Mayo* test was announced and began to be extensively applied, the courts and the USPTO have tried to consistently distinguish between patent-eligible subject matter and subject matter falling within a judicial exception. Even so, patent stakeholders have expressed a need for more clarity and predictability in its application. In particular, stakeholders have expressed concern with the proper scope and application of the "abstract idea" exception. Some courts share these concerns, for example as demonstrated by several recent concurrences and dissents in the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") calling for changes in the application of Section 101 jurisprudence.[2] Many stakeholders, judges, inventors, and practitioners across the spectrum have argued that something needs to be done to increase clarity and consistency in how Section 101 is currently applied.

To address these and other concerns, the USPTO is revising its examination procedure with respect to the

2. *See, e.g., Interval Licensing LLC* v. *AOL, Inc.,* 896 F.3d 1335, 1348 (Fed. Cir. 2018) (Plager, J., concurring in part and dissenting in part); *Smart Sys. Innovations, LLC* v. *Chicago Transit Auth.*, 873 F.3d 1364, 1377 (Fed. Cir. 2017) (Linn, J., dissenting in part and concurring in part); *Berkheimer* v. *HP Inc.,* 890 F.3d 1369, 1376 (Fed. Cir. 2018) (Lourie, J., joined by Newman, J., concurring in denial of rehearing en banc).

first step of the *Alice/Mayo* test[3] (Step 2A of the USPTO's Subject Matter Eligibility Guidance as incorporated into the Manual of Patent Examining Procedure ("MPEP") 2106)[4] by: (1) Providing groupings of subject matter that is considered an abstract idea; and (2) clarifying that a claim is not "directed to" a judicial exception if the judicial exception is integrated into a practical application of that exception.

Section I of this 2019 Revised Patent Subject Matter Eligibility Guidance explains that the judicial exceptions are for subject matter that has been identified as the "basic tools of scientific and technological work,"[5] which includes "abstract ideas" such as mathematical concepts, certain methods of organizing human activity, and mental processes; as well as laws of nature and natural phenomena. Only when a claim recites a judicial exception does the claim require further analysis in order to determine its eligibility. The groupings of abstract ideas contained in this guidance enable USPTO personnel to

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3. The first step of the *Alice/Mayo* test is to determine whether the claims are "directed to" a judicial exception. *Alice,* 573 U.S. at 217 (citing *Mayo,* 566 U.S. at 77).

4. All references to the MPEP in the 2019 Revised Patent Subject Matter Eligibility Guidance are to the Ninth Edition, Revision 08-2017 (rev. Jan. 2018), unless otherwise indicated.

5. *Mayo,* 566 U.S. at 71 ("Phenomena of nature, though just discovered. mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work" (quoting *Gottschalk* v. *Benson,* 409 U.S. 63, 67 (1972)).

more readily determine whether a claim recites subject matter that is an abstract idea.

Section II explains that the USPTO has set forth a revised procedure, rooted in Supreme Court caselaw, to determine whether a claim is "directed to" a judicial exception under the first step of the *Alice/Mayo* test (USPTO Step 2A).

Section III explains the revised procedure that will be applied by the USPTO. The procedure focuses on two aspects of Revised Step 2A: (1) Whether the claim recites a judicial exception; and (2) whether a recited judicial exception is integrated into a practical application. Only when a claim recites a judicial exception and fails to integrate the exception into a practical application, is the claim "directed to" a judicial exception, thereby triggering the need for further analysis pursuant to the second step of the *Alice/Mayo* test (USPTO Step 2B). Finally, if further analysis at Step 2B is needed (for example to determine whether the claim merely recites well-understood, routine, conventional activity), this 2019 Revised Patent Subject Matter Eligibility Guidance explains that the examiner or administrative patent judge will proceed in accordance with existing USPTO guidance as modified in April 2018.[6]

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6. USPTO Memorandum of April 19, 2018. "Changes in Examination Procedure Pertaining to Subject Matter Eligibility, Recent Subject Matter Eligibility Decision *(Berkheimer* v. *HP, Inc.*)" (Apr. 19, 2018), *available at https://www.uspto.gov/sites/default/files/documents/memo-berkheimer-20180419.PDF* [hereinafter "USPTO *Berkheimer* Memorandum").

Appendix A

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- an additional element that applies or uses a judicial exception to effect a particular treatment or prophylaxis for a disease or medical condition;[26]

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26. For example, an immunization step that integrates an abstract idea into a specific process of immunizing that lowers the risk that immunized patients will later develop chronic immune-mediated diseases. *See, e.g., Classen Immunotherapies, Inc. v. Biogen IDEC*, 659 F.3d 1057, 1066-68 (Fed. Cir. 2011). *See also Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1135 (Fed. Cir. 2018) (holding claims to the practical application of the natural relationships between iloperidone, CYP2D6 metabolism, and QTc prolongation to treat schizophrenia, not merely the recognition of those relationships, to be patent eligible at *Mayo/Alice* step 1 (USPTO Step 2A)), and USPTO Vanda Memorandum (discussing *Vanda*).

APPENDIX B — UNITED STATES PATENT AND TRADEMARK OFFICE AMENDMENT TO NON-FINAL REJECTION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants(s): Curt D. Wolfgang, *et al.*

Conf. No.: 7411

Serial No.: 11/576,178

Art Unit: 1634

Filed: March 28, 2007

Examiner: Diana B. Johannsen

Examiner: VAND-0002-US

Title: **Methods for the Administration of Iloperidone**

Date: March 20, 2013

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Appendix B

AMENDMENT TO NON-FINAL REJECTION

Sir:

I. INTRODUCTORY COMMENTS

This paper is in response to the non-final Office Action dated December 20, 2012. Please amend the above-referenced patent application as follows:

The Amendments to the Claims are reflected in the listing of the claims that begins on page 2 of this paper.

Remarks begin on page 7 of this paper.

The Conclusion appears on page 18 of this paper.

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None of Jain, Woosley, or Neville cures or is alleged to cure the above-discussed deficiencies in Obach. As noted in the Office Action, "Jain does not teach the administration of iloperidone to a subject who 'is a CYP2D6 poor metabolizer' or to a subject who 'is at risk for iloperidone-induced QTc prolongation'" (Office Action, p. 6.) Rather, "Jain provides an overview of several studies of iloperidone, teaching that daily dosages of iloperidone up to 24 mg/day have been 'found to be well tolerated' (citation omitted), as well as clinical trials in which iloperidone was administered at dosages of 4 and 8 mg/day and at 0.25 - 3 mg b.i.d. (citation omitted). Jain also discloses a long term study of dosages of 4-16 mg/day

(citation omitted), as well as the finding of efficacy at a dosage of 8 mg/day, and tolerance of a dosage of 32 mg/day (citation omitted)." (Office Action, p. 5.) These teachings, even in combination with Obach's, fail to disclose or even hint at the claimed methods, including "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 has a CYP2D6 normal metabolizer genotype or a CYP2D6 extensive 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 that is greater than 12 mg/day, up to 24 mg/day" (claim 63), "internally administering iloperidone to [a patient who is suffering from a psychotic disorder and is a CYP2D6 poor metabolizer] in an amount of up to 12 mg/day" (claim 71), and "internally administering iloperidone to [a patient who is suffering from a psychotic disorder and who is at risk for iloperidone-induced QTc prolongation] in an amount of up to 12 mg/day" (claim 77).

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