No. 19-

IN THE

Supreme Court of the United States

INO THERAPEUTICS LLC, MALLINCKRODT HOSPITAL PRODUCTS INC., MALLINCKRODT HOSPITAL PRODUCTS IP LTD.,

Petitioners,

v.

PRAXAIR DISTRIBUTION INC., PRAXAIR INC.,

Respondents.

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

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Whether a method of treatment that requires doctors to selectively administer a drug to certain patients and not others to enhance patient outcomes is eligible for patent protection under Section 101 of the Patent Act.

CORPORATE DISCLOSURE STATEMENT

Mallinckrodt Hospital Products IP Ltd. is a private limited company formed under the laws of Ireland. The direct parent corporation of Mallinckrodt Hospital Products IP Ltd. is Mallinckrodt IP Unlimited Company, a private unlimited company formed under the laws of Ireland. The ultimate parent of Mallinckrodt Hospital Products IP Ltd. is Mallinckrodt plc, a public limited company incorporated and organized under the laws of Ireland. No other publicly held corporation owns 10 percent or more of Mallinckrodt Hospital Products IP Ltd.

INO Therapeutics LLC is a wholly owned subsidiary of Therakos, Inc., which is a wholly owned subsidiary of Mallinckrodt Hospital Products Inc. Mallinckrodt Hospital Products Inc., which is the successor by merger to Ikaria, Inc., is an indirect wholly owned subsidiary of Mallinckrodt plc, a public limited company incorporated and organized under the laws of Ireland. No other publicly held corporation owns 10 percent or more of Mallinckrodt Hospital Products Inc. or INO Therapeutics LLC.

TABLE OF CONTENTS

TABLE OF CONTENTS—Continued

TABLE OF AUTHORITIES

CASES

TABLE OF AUTHORITIES—Continued

DOCKETED CASES

CONSTITUTIONAL AND STATUTORY PROVISIONS

REGULATIONS AND LEGISLATIVE MATERIALS

TABLE OF AUTHORITIES—Continued

OTHER AUTHORITIES

TABLE OF AUTHORITIES—Continued

OPINIONS BELOW

The opinion of the Federal Circuit (App. 1a-35a) is reported at 782 F. App'x 1001. The Federal Circuit's order denying rehearing en banc (App. 99a-100a) is unreported. The district court's memorandum containing its findings of facts and conclusions of law (App. 37a-98a) is unreported.

JURISDICTION

The Federal Circuit entered judgment on August 27, 2019. That court denied Mallinckrodt's timely petition for rehearing en banc on November 19, 2019. This Court has jurisdiction under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

Section 101 of Title 35 of the United States Code 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." Section 100(b) of Title 35 of the United States Code provides: "The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."

INTRODUCTION

In the years since this Court's decision in *Mayo Collaborative Services* v. *Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), the lower courts have struggled to apply the judicially-created exceptions to the subject matter that Congress declared eligible for patent protection in 35 U.S.C. § 101. The decision below takes that uncertainty to a new level by holding for the

first time that a method of selectively treating patients with a drug based on the results of a diagnostic step is ineligible for patent protection even if it meets all the other requirements of the statute. That holding threatens important medical advances and strays ever further from the text that Congress drafted. There is no more pressing issue in patent law than resolving the uncertainty that has surrounded the judicial exceptions to § 101. With this latest expansion, the time has come for this Court to provide badly needed guidance.

The Federal Circuit has openly called for this Court's help interpreting § 101. Multiple judges have written separate opinions raising alarms about the unsettled state of the law. In 2015, Judge Lourie (joined by Judge Moore) warned that "a crisis of patent law and medical innovation may be upon us." *Ariosa Diagnostics, Inc.* v. *Sequenom, Inc.*, 809 F.3d 1282, 1285 (Fed. Cir. 2015) (concurring in denial of rehearing en banc). Judge Dyk likewise predicted that the Federal Circuit's expansive application of *Mayo* "may discourage development and disclosure of new diagnostic and therapeutic methods in the life sciences" but found that "any further guidance must come from the Supreme Court, not [the Federal Circuit.]" *Id.* at 1287 (concurring in denial of rehearing en banc).

More recently, in *Athena Diagnostics, Inc.* v. *Mayo Collaborative Services, LLC*, 927 F.3d 1333, 1367-1368 (Fed. Cir. 2019) (*cert. denied*, No. 19-430 (U.S. Jan. 13, 2020)), the en banc Federal Circuit issued eight separate opinions on its decision to deny en banc review. Although a slight majority of the en banc Federal Circuit thought *Mayo* rendered medical diagnostic methods ineligible for patent protection, all members of the court of appeals believed that to be the wrong result. The broad consensus was that the Federal Circuit

needed this Court's assistance to resolve the confusion created by *Mayo*'s conflicting messages.

In the *Athena* en banc majority, Judge Lourie (joined by Judges Reyna and Chen) reiterated his prior "concerns over current precedent" but concluded the Federal Circuit "can accomplish little" without intervention from this Court or Congress. 927 F.3d at 1335-1336. Judge Hughes (joined by Chief Judge Prost and Judge Taranto) agreed that the multiple concurring and dissenting opinions "are illustrative of how fraught the issue of § 101 eligibility" has become, and that "this is not a problem that [the Federal Circuit] can solve." *Id.* at 1337. Judge Dyk (joined by Judge Hughes, and by Judge Chen in part) highlighted the tensions between this Court's decisions and urged "the Supreme Court to refine the *Mayo* framework." *Id.* at 1340. Judge Chen, in a fourth concurrence, explained that *Mayo* set forth a test "which is a more far-reaching, aggressive version of the [prior] judicial exceptions to the statute" and stated that the Federal Circuit "would benefit from the Supreme Court's guidance." *Id.* at 1344.

The five *Athena* dissenters agreed with the majority that the Federal Circuit's application of *Mayo* needed to be corrected. For example, Judge Newman's dissent (joined by Judge Wallach) concluded that the Federal Circuit's "section 101 jurisprudence warrants attention" and "Federal Circuit precedent is ripe for reconsideration … to correct our application of the *Mayo* decision and to restore the necessary economic incentive" for pursuing "'medical advances like life-saving precision medicine and diagnostics.'" 927 F.3d at 1370. Judge Moore (joined by Judges O'Malley, Wallach, and Stoll) decried the Federal Circuit's erroneous conversion of *Mayo* into a rigid, "per se rule that diagnostic kits and techniques are ineligible." *Id.* at 1354. Their

message to litigants was clear: "No need to waste resources with additional en banc requests. Your only hope lies with the Supreme Court or Congress." *Id.* at 1363.

The United States has joined this chorus. In a brief invited by this Court, it explained in unflinching terms the conflicting signals that have been sent and the "important and recurring questions on which the Court's recent Section 101 decisions have fostered substantial uncertainty." U.S. Br. 8, *Hikma Pharm. USA Inc.* v. *Vanda Pharm. Inc.*, No. 18-817 (U.S. Dec. 6, 2019). It warned that although the patent eligibility of "method-of-treatment claims has long been settled," the "rote application of the *Mayo* two-step framework" might "call into question such bedrock understandings of the patent system, in a way that the *Mayo* Court clearly did not envision." *Id.* at 14. Thus, although it deemed the case before it a bad vehicle because the Federal Circuit had upheld the method-of-treatment claim, the United States concluded that "further guidance from this Court is amply warranted" and should be provided "in a case where the current confusion has a material effect on the outcome of the Section 101 analysis." *Id.* at 22-23.

This is just such a case. The one island of stability to have emerged from the general confusion surrounding the question of patent-eligible subject matter had been that method-of-treatment claims are the type of subject matter eligible for patent protection. But as the United States warned, even that refuge was not safe. The decision below blurs the line between methods-of-treatment claims and diagnostic claims, holding for the first time that a method of selectively treating patients that applies a diagnostic step does not even meet the threshold requirement of patent eligibility.

With that ruling, the Federal Circuit has extended the judicially created exceptions to the plain text of 35 U.S.C. § 101 far beyond anything envisioned by this Court. The petition for a writ of certiorari should be granted to rein in the Federal Circuit's runaway jurisprudence, which threatens innovations at the forefront of medical science.

STATEMENT

A. Judicially-Created Exceptions To Section 101

This case addresses the important question of what types of inventions may be claimed in a patent. Concluding that a claim's subject matter is eligible for patent protection does not mean that a patent will be granted. Subject-matter eligibility is merely a threshold question. Many other requirements—including that the claim be novel, 35 U.S.C. § 102, non-obvious, *id.* § 103, and described adequately to enable its use, *id.* § 112—must be met before a patent is granted.

Congress used broad language to describe the subject matter eligible for patent protection. Section 101 of the Patent Act provides that "[w]hoever 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." 35 U.S.C. § 101. An "invention" means "invention or discovery," and "process" includes "a new use of a known process, machine, manufacture, composition of matter, or material." *Id.* § 100(b). Section 101 is "cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and … useful Arts' with all that means for the social and economic

benefits." *Diamond* v. *Chakrabarty*, 447 U.S. 303, 315 (1980) (quoting U.S. Const. art. I, § 8.).

This Court has limited Section 101's plain text with implicit exceptions to patent eligibility for "laws of nature, natural phenomena, and abstract ideas," on the premise that such discoveries are "'manifestations of … nature, free to all men and reserved exclusively to none.'" *Diamond* v. *Diehr*, 450 U.S. 175, 185 (1981). Accordingly, "'[a] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter,'" and "'Einstein could not patent his celebrated law that E=mc2.'" *Id.*

At the same time, the Court has repeatedly cautioned that "too broad an interpretation of this exclusionary principle could eviscerate patent law," "[f]or all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas." *Mayo*, 566 U.S. at 71. Thus, while a process may not "too broadly preempt the use of a natural law," it is also "'not unpatentable simply because it contains a law of nature.'" *Id.* at 71-72. Rather, "an *application* of a law of nature" even "to a known structure or process may well be deserving of patent protection." *Diehr*, 450 U.S. at 187.

Several years ago, the Court established a two-step framework for determining the threshold question of whether a patent claims subject matter that is eligible for patent protection. At step one, a court inquires "whether the claims at issue are directed to [a] patent-ineligible concept[]." *Alice Corp.* v. *CLS Bank Int'l*, 573 U.S. 208, 217 (2014). If the claims are not directed to such a concept, the subject matter of the claims is eligible for patent protection. If they are, the court searches for an "'inventive concept'" that would confer

patent eligibility—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.'" *Id.* at 217-218 (alteration in original).

Applying that framework in *Mayo*, the Court held that a medical diagnostic claim failed to "transform[] … unpatentable natural laws into patent-eligible applications of those laws." 566 U.S. at 72. The representative claim required determining a metabolite level in a patient's blood, "'wherein the level of'" the metabolite "'indicates a need to increase'" or "'indicates a need to decrease'" the amount of drug administered to the patient. *Id.* at 75. Importantly, the claim merely "'indicate[d] a need to decrease' (or 'to increase')," and was "not limited to instances in which the doctor actually decreases (or increases) the dosage level where the test results suggest that such an adjustment is advisable." *Id.* at 75-76 (citing patentee's brief, which described using the "'measurements to *inform* the calibration'" of dosages). Thus, the patentee failed to "do more than simply state the law of nature while adding the words 'apply it.'" *Id.* at 72; *see also id.* at 82 ("[T]he effect is simply to tell doctors to apply the law somehow when treating their patients.").

Mayo carefully distinguished the claims before it from method of treatment claims, which it indicated should remain patent-eligible as specific applications of natural phenomena. The ineligible claims were "[u]nlike … a typical patent on a new drug or a new way of using an existing drug [because] the patent claims do not confine their reach to particular applications of those laws." 566 U.S. at 87. Specifically, by attempting to cover all subsequent treatment activity once the doctor considered the natural correlations,

"whether that treatment does, or does not, change in light of the inference he has drawn using the correlations," the ineligible claims "threaten to inhibit the development of more refined treatment recommendations" based on "later discovered features of metabolite, human physiology or individual patient characteristics." *Id.* at 86-87.

B. Mallinckrodt's Patents

Mallinckrodt manufactures and markets INOmax®, which is a gaseous blend of nitric oxide and nitrogen that was approved in 1999 for treatment of term and near-term neonates experiencing hypoxic respiratory failure. C.A.J.A. 181(1:20-24). INOmax® was initially contraindicated only for certain patients. C.A.J.A. 182 (3:53-56).

In 2004, Mallinckrodt sponsored a clinical study—called the INOT22 study—to further assess the safety and efficacy of inhaled nitric oxide. C.A.J.A. 25829-25830. That study included a class of patients with left ventricular dysfunction ("LVD")—i.e., problems with the left ventricle that lead to an increase in pressure in the left atrium of the heart. No clinical trial prior to Mallinckrodt's study excluded patients with LVD from treatment with inhaled nitric oxide. C.A.J.A. 2429, 25830. Indeed, although Mallinckrodt's study protocol was evaluated by more than 115 professionals experienced in the review of clinical trial protocols, no one suggested that patients with LVD should be excluded from the study. C.A.J.A. 25161, 25830.

After several patients experienced adverse events, Mallinckrodt developed a new treatment protocol in which patients determined to have pre-existing LVD based on a pulmonary capillary wedge pressure greater

than 20 mmHg were excluded from treatment with inhaled nitric oxide. C.A.J.A. 185(9:48-54), 187(14:17-21). Mallinckrodt's new treatment protocol resulted in a 90% reduction in severe adverse events. C.A.J.A. 25830.

Mallinckrodt obtained U.S. Patent 8,795,741 ("the '741 patent") on this new method of selective treatment. Claim 1, on which the Federal Circuit focused its analysis, claimed a "method of treating patients" that reduces the risk that treatment will "lead[] to pulmonary edema in neonatal patients with hypoxic respiratory failure." C.A.J.A. 187(14:28-33). The method begins with "identifying a plurality of term or near-term neonatal patients" with hypoxic respiratory failure. C.A.J.A. 187(14:34-36). Next, the method recites two related steps of "determining that a first patient of the plurality does not have left ventricular dysfunction," and "determining that a second patient of the plurality has left ventricular dysfunction, so is at particular risk of increased [pulmonary capillary wedge pressure] leading to pulmonary edema upon treatment with inhaled nitric oxide." C.A.J.A. 187(14:37-42). Finally, the method requires doctors to take two specific steps based on those prior determinations: selectively "administering 20 ppm inhaled nitric oxide treatment to the first patient"; but "excluding the second patient from treatment with inhaled nitric oxide"—i.e., dropping the dose all the way to 0 ppm. C.A.J.A. 187(14:43-49).

Claim 1 thus includes both diagnostic steps and treatment steps. The diagnostic steps require categorization of patients based on whether they have LVD. The treatment steps that follow require the selective administration of inhaled nitric oxide based on whether a patient has pre-existing LVD.

C. The Proceedings Below

Mallinckrodt brought a patent infringement action against Praxair Distribution Inc. and Praxair Inc. (collectively, "Praxair") for, among other things, infringement of the '741 patent based on Praxair's filing of an Abbreviated New Drug Application seeking approval to market its generic inhaled nitric oxide products based on the INOmax® label. The district court found the asserted claims were ineligible under § 101.

On appeal, a divided panel of the Federal Circuit held that Mallinckrodt's selective treatment claims are not patent-eligible subject matter. App. 9a. Starting from the premise that the effect of inhaled nitric oxide on a newborn with LVD is a natural law, the majority concluded that the claim is "'directed to' a natural phenomenon." *Id.* In the majority's view, "the claim is directed to detecting the presence of LVD in a patient and then," for those patients with LVD, "doing nothing but leaving the natural processes taking place in the body alone." App. 10a. The majority attempted to distinguish its precedent in *Vanda Pharmaceuticals Inc.* v. *West-Ward Pharmaceuticals Int'l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018), *cert. denied*, No. 18-817 (U.S. Jan. 13, 2020), which held that a method of selective treatment was patent-eligible, on the ground that claims in *Vanda* "did not simply instruct doctors to stop treating those patients" but "required the doctor to *treat* a patient with a specific low-dose range." App. 12a.

At step two of the *Alice* analysis, the majority concluded that each element of the claims apart from the natural law was conventional. App. 18a-20a. In the majority's view, the claimed combination of treating patients without LVD with an existing dosage while withholding inhaled nitric oxide from patients with

LVD "amounts to little more than an instruction to doctors to 'apply' the applicable law when treating their patients." App. 21a.

Judge Newman dissented. Citing *Mayo* and the Federal Circuit's precedent in *Vanda*, she noted that the majority had deviated from precedent holding that methods of medical treatment are eligible for patent protection. App. 29a. She warned, "Today's change of law adds to the inconsistency and unpredictability of this area of patent-supported innovation." *Id.* She also explained that despite the majority's attempt to characterize its holding as narrow, "[t]his disclaimer appears at the end of a lengthy exposition, whose wide-ranging pronouncements of law and policy are not tied to narrow circumstances or claims." App. 33a. "The majority's broad pronouncement of ineligibility of medical treatment that relates to human physiology," she continued, "not only contravenes precedent, but contravenes the national interest in achieving new methods of medical treatment with the assistance of the patent incentive." App. 33a-34a.

REASONS FOR GRANTING THE PETITION

I. THE FEDERAL CIRCUIT'S DECISION HEIGHTENS THE CONFUSION IN THE LOWER COURTS ON A QUESTION OF NATIONAL IMPORTANCE

The traditional understanding that methods of treatment are eligible for patent protection had provided a rare point of certainty amid substantial confusion and disagreement about how to apply the judicially-created exceptions to § 101. The decision below erodes that certainty by holding that a method of selectively administering a drug is not patent-eligible subject matter. The decision thus deepens the urgent need for this

Court's guidance on the important threshold question of what subject matter is eligible for patent protection.

A. The Scope Of The Judicial Exceptions To Section 101 Has Generated Substantial Confusion

The Federal Circuit has struggled for years to apply the judicial exceptions to § 101. The vast majority of judges on the Federal Circuit have expressly called on this Court to clarify the law in this area. They have noted inconsistencies in this Court's precedent and disputed among themselves how to interpret and apply the framework created by this Court.

This confusion was on full display when the Federal Circuit split 7-5 on the patent eligibility of diagnostic claims in *Athena Diagnostics, Inc.* v. *Mayo Collaborative Servs., LLC*, 927 F.3d 1333 (Fed. Cir. 2019) (*cert. denied*, No. 19-430 (U.S. Jan. 13, 2020)). Judge Lourie (joined by Judges Reyna and Chen) expressed "concerns over current precedent." *Id.* at 1335. Judge Hughes (joined by Chief Judge Prost and Judge Taranto) said that "the issue of § 101 eligibility" has become "fraught" with problems the Federal Circuit cannot solve as "an inferior appellate court." *Id.* at 1337. Judge Moore (joined by Judges O'Malley, Wallach, and Stoll) expressed doubt that "the Supreme Court intended *Mayo* to be the sweeping decision it has become." *Id.* at 1363. Judge Newman likewise concluded that the Federal Circuit has "mistakenly enlarged" the exceptions created by this Court. *Id.* at 1364. Judge O'Malley questioned how far the current state of the law has drifted from the statutory text. *Id.* at 1371. And Judge Chen, who previously served as Solicitor of the Patent and Trademark Office, observed that the present state of the law is "a very difficult thing to ex-

plain to 8,000 patent examiners" because it has become "highly subjective and impressionistic" and "puts courts and examiners in the position of assigning value judgments." *Id.* at 1349.

Athena was by no means the first case in which the Federal Circuit has expressed confusion and division on patent eligibility or called for this Court's intervention. In 2018, Judge Plager observed that the "incoherent body of doctrine" surrounding Section 101 "renders it near impossible to know with any certainty whether [an] invention is or is not patent eligible," and that "the state of the law is such as to give little confidence" in the court's decisions. *Interval Licensing LLC* v. *AOL, Inc.*, 896 F.3d 1335, 1348 (Fed. Cir. 2018) (Plager, J., concurring-in-part and dissenting-in-part).

Judge Linn has similarly observed that Section 101 jurisprudence "is indeterminate and often leads to arbitrary results." *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); *see also Ariosa Diagnostic, Inc.* v. *Sequenom, Inc.*, 788 F.3d 1371, 1381 (Fed. Cir. 2015) (Linn, J., concurring) (concurring in a decision invalidating patent claims even though he "s[aw] no reason, in policy or statute, why th[e] breakthrough invention [at issue] should be deemed patent ineligible").

Judges Lourie and Newman have also remarked previously that "the law needs clarification by higher authority." *Berkheimer* v. *HP Inc.*, 890 F.3d 1369, 1374 (Fed. Cir. 2018) (Lourie and Newman, JJ., concurring in the denial of rehearing en banc) (*cert. denied*, No. 18-415 (U.S. Jan. 13, 2020)).

This collective and consistent cry for help from the Federal Circuit is extraordinary and emphasizes just

how critical this Court's guidance is. Patent eligibility is a threshold question of enormous importance to innovation and the economy, and the judges tasked with hearing all patent appeals in the United States have now told this Court in no uncertain terms that they are confused and need clarification on how to apply those judicial exceptions.

The United States, retired judges, government officials, practitioners, and commentators have all echoed and amplified the need for guidance from this Court. In its invitation brief in *Hikma Pharmaceuticals USA Inc.* v. *Vanda Pharmaceuticals Inc.*, No. 18-817 (U.S. Dec. 6, 2019), the United States argued that this Court's "reconceptualization" of traditional "limitations on Section 101's affirmative scope as freestanding, atextual 'exceptions,' has given rise to an array of difficult questions." U.S. Br. 8. Those "important and recurring questions," it noted, "warrant[] review in an appropriate case." *Id.*

Paul Michel, the retired Chief Judge of the Federal Circuit, testified to Congress that Section 101 "case law ha[s] produced unending chaos." Michel Testimony 1, *The State of Patent Eligibility in America, Part I: Hearing Before the Subcomm. on Intellectual Property of the S. Comm. on the Judiciary*, 116th Cong. (June 4, 2019), https://bit.ly/2WEZugp. He explained that "[b]ecause court decisions are so unpredictable," patents have become "unreliable" and "no longer sufficiently incentivize the large investments in research and development in new technologies our nation needs." *Id.* "Massive uncertainty," he further noted, "pervades all determinations, whether by 8,300 patent examiners, 1,000 federal trial judges, or 18 Federal Circuit judges." *Id.* at 5. He explained:

> recent cases are unclear, inconsistent with one another and confusing. I myself cannot reconcile the cases. … Nor can I predict outcomes in individual cases with any confidence since the law keeps changing year after year. If I, as a judge with 22 years of experience deciding patent cases on the Federal Circuit's bench, cannot predict outcomes based on case law, how can we expect patent examiners, trial judges, inventors and investors to do so?

Id. at 2.

Current and former directors of the U.S. Patent and Trademark Office agree with this assessment. PTO Director Andrei Iancu declared that the interpretation of Section 101 is "'the most important substantive patent law issue in the United States today. And it's not even close.'" Davis, *Courts Can Resolve Patent Eligibility Problems, Iancu Says*, Law360 (Apr. 11, 2019), https://bit.ly/2mdkE4J. He further noted that "'[r]ecent case law has created significant confusion'" that "'must be addressed now.'" Nurton, *Iancu Calls on Federal Circuit to Fix Section 101 Problem*, IP Watchdog (May 2, 2019), https://bit.ly/2lQECSg. Former PTO Director David Kappos testified that "patent eligibility law truly is a mess" with courts and the PTO "spinning their wheels on decisions that are irreconcilable, incoherent, and against our national interest." Kappos Testimony 1-2, *State of Patent Eligibility, Part I* (June 4, 2019), https://bit.ly/2K3JjTW. His predecessor, Q. Todd Dickinson, testified that "the current rules are unnecessarily ambiguous and uncertain, and this uncertainty ends up serving no one." Dickinson Testimony 7, *State of Patent Eligibility, Part I* (May 5, 2019), https://bit.ly/2mUmFn3.

The Federal Circuit's wavering hand has only made the PTO's struggle implementing this Court's Section 101 case law more difficult. As the PTO explained, "[t]he growing body of precedent [from the Federal Circuit] has become increasingly more difficult for examiners to apply in a predictable manner, and concerns have been raised that different examiners within and between technology centers may reach inconsistent results." 84 Fed. Reg. 50, 52 (Jan. 7, 2019).

Practitioners have also pointed out that the current Section 101 standard "ha[s] created significant uncertainty about what is eligible for patenting." *State of Patent Eligibility, Part II*, at 2 (June 5, 2019) (testimony of Barbara Fiacco, President-Elect of the American Intellectual Property Law Ass'n), https://bit.ly/2ZeVrFb. That uncertainty has, in turn, "reduced investment in new technologies, produced inconsistency and uncertainty about patent rights and their enforceability, cast a cloud over licensing and other intellectual property transactions, and driven industry to foreign jurisdictions." *Id.*

The American Bar Association has expressed the same concerns that "the current jurisprudence on patent eligibility … is confusing, creates uncertainty as to the availability and enforceability of patent assets, arguably risks the incentive to innovate provided by patents in technologies …, and potentially places the U.S. in a less advantageous position on patent protection than our leading competitor nations." ABA, *Comments Related to Patent Subject Matter Eligibility* 2 (Jan. 18, 2017), https://bit.ly/2mbtoIr.

Scholars and commentators have likewise observed that "[t]he law of patentable subject matter is a mess," and that the Federal Circuit's "inconsistent and uncer-

tain" application of Section 101 seems to be getting only "less, not more, certain over time." *State of Patent Eligibility, Part I*, at 1-2 (June 4, 2019) (testimony of Prof. Mark Lemley, Stanford Law School), https://bit.ly/2n8tH7x. This "uncertainty," they have warned, "has imposed a substantial cost on society" by making it "extreme[ly] difficult[] … for innovators and investors … to discern the validity of their existing patents and the availability of meaningful protection for future innovations." Holman, *Patent Eligibility Post-Myriad: A Reinvigorated Judicial Wildcard of Uncertain Effec*t, 82 Geo. Wash. L. Rev. 1796, 1830 (2014).

B. The Decision On Review Exacerbates The Uncertainty In The Lower Courts

Amid this chaos, one area of relative certainty had been that method-of-treatment claims would be considered patent-eligible. As the United States explained, "[h]istorically, it was well understood" that "methods of medical treatment" are patent-eligible. *Hikma*, U.S. Br. 9-10. This understanding was applied by the Federal Circuit in *Vanda* to uphold a claim that required doctors to adjust the dose of a particular drug downward (to "12 mg/day or less") if genetic testing showed that the patient was likely to poorly metabolize the drug. *Vanda Pharm. Inc.* v. *West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1121 (Fed. Cir. 2018), *cert. denied*, No. 18-817 (U.S. Jan. 13, 2020).

Other decisions of the Federal Circuit have also upheld method-of-treatment claims. *See, e.g.*, *Natural Alternatives Int'l, Inc.* v. *Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019) (claims reciting provision of dietary supplements to increase an athlete's anaerobic working capacity are directed to patent-eligible methods of treatment); *Endo Pharm. Inc.* v. *Teva*

Pharm. USA, Inc., 919 F.3d 1347 (Fed. Cir. 2019) (claims requiring doctors to adjust the dosage of a drug for certain patients are directed to a patent-eligible treatment method).

The decision below breaches that firewall, holding for the first time that a method of selective treatment is not patent-eligible. The Federal Circuit tried to finesse that point by arguing that the "excluding" step in Mallinckrodt's claims was an instruction "*not* to act," rather than "a new way of *treating* LVD patients." App. 10a. But even if excluding a patient from inhaled nitric oxide can be deemed inaction, that is not what Mallinckrodt claimed. Instead, it drafted its claims to cover an integrated treatment protocol. Those claims are infringed only when a doctor determines that one patient has LVD while another does not, and then actually treats the second patient with 20 ppm of inhaled nitric oxide while withholding treatment from the first "based on the determination" regarding LVD. Mallinckrodt's claims are thus not directed to inaction, but to *selective* action: the selective administration of inhaled nitric oxide based on a diagnostic step.

The decision that such claims do not even pass the threshold requirement for patent protection casts a cloud of uncertainty over an entire category of important innovation. Selective treatment claims, like Mallinckrodt's, are not simply diagnostic methods designed to generate information about a physiological condition. They *apply* that knowledge to achieve remarkable improvements in health through specific, real world action.

The Federal Circuit's blurring of that critical distinction will have dire consequences and adds to the already substantial uncertainty in this area of the law.

The government feared such results when it said that "it is arguably unclear how the longstanding and entirely correct rule that method-of-treatment claims are patent-eligible can be reconciled with mechanical application of *Mayo*'s two-step framework." *Hikma*, U.S. Br. 10. And it represents a "change of law" that "adds to the inconsistency and unpredictability of this area of patent-supported innovation." App. 29a (Newman, J., dissenting).

Moreover, although the decision most immediately impacts selective treatment claims, that is not where the effect of the panel's decision is likely to stop. The broad principle that patent protection is not available for methods that selectively perform or withhold a step previously performed indiscriminately has wide-ranging implications. It could reach, for example, manufacturing processes in which testing and predefined criteria are used to determine whether a step previously performed on all batches can be skipped in some instances, increasing efficiency and reducing the problems that come with over-processing.

The time has come for this Court to take action. The exceptions it created to the plain text of Section 101 are being misapplied with a breadth this Court never imagined. After declaring diagnostic methods effectively unpatentable while calling for this Court's guidance, the Federal Circuit has expanded the exceptions once again. At stake are billions of dollars in investment decisions and the potential loss of important breakthroughs in medicine and beyond.

II. THE FEDERAL CIRCUIT'S DECISION IS WRONG

The United States has urged this Court to clarify the law of patent eligibility "in an appropriate case" in which "the current confusion has a material effect on

the outcome of the Section 101 analysis." *Hikma*, U.S. Br. 8, 22. This is that case.

The capacious language of Section 101 provides that "[w]hoever 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." 35 U.S.C. § 101. The language chosen by Congress easily encompasses Mallinckrodt's claims. This case thus turns entirely on judicially-created exceptions, unsupported by the statutory text.

Nothing in this Court's precedent supports the Federal Circuit's invalidation of Mallinckrodt's selective treatment claims under one of those judicial exceptions. The claim in *Mayo* was an oddity and easily distinguishable. It recited a method of (a) administering a thiopurine drug to a patient and then (b) determining the metabolite levels. The claim then concluded with two "wherein" clauses reciting the fact that certain levels indicated increasing or decreasing the dosage. 566 U.S. at 74-75. Even before the patent, scientists already performed the first two steps, "routinely measur[ing] metabolites as part of their investigations into the relationships between metabolite levels and efficacy and toxicity of thiopurine [drugs]." *Id.* at 73-74, 79. The two "wherein" clauses thus merely revealed certain *information* to a "pre-existing audience." *Id.* at 78. Critically, the claim did not require doctors to *act on* that information, merely "trusting them to use those laws appropriately where they are relevant to their decisionmaking." *Id.* at 78. This Court concluded that such an instruction to "consider" diagnostic information was not patent-eligible because it "tie[d] up the doctor's subsequent treatment decision *whether that treatment*

does, or does not, change." *Id.* at 86-87 (emphasis added).

The "excluding" step in Mallinckrodt's claims, by contrast, does change the course of treatment by requiring selective administration of inhaled nitric oxide. Indeed, selective administration is capable of reducing severe adverse events by as much as 90%, C.A.J.A. 2391-2392, whereas the "wherein" clauses in *Mayo* did not necessarily change, let alone improve, treatment outcomes, 566 U.S. at 78, 86-87.

The Federal Circuit lost sight of this critical distinction between merely reciting and actually applying a natural law by improperly dissecting the claims. As this Court has explained, "[i]n determining the eligibility of [parties'] claimed process for patent protection under § 101, their claims must be considered as a whole. It is inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." *Diamond* v. *Diehr*, 450 U.S. 175, 188 (1981). The majority's focus on the "excluding" step, rather than viewing the claim as a whole, caused it to ignore the fact that Mallinckrodt had not claimed a natural law but rather an integrated treatment protocol involving selective administration of a drug guided by a diagnostic step.

The Federal Circuit's attempt to distinguish *Vanda*, in which the author of the opinion in this case had dissented, was also unavailing. The majority attempted to draw a bright line between treating and not treating by arguing that the diagnostic step in *Vanda* led doctors to administer a lower dose, rather than no dose, to patients for whom conventional treatment was deemed inappropriate. Neither the statute nor this Court's case law supports such arbitrary distinctions. A meth-

od of administering the normal dosage of a drug to certain patients while administering *none* to others is just as much a treatment protocol as a method of administering the normal dosage of a drug to certain patients while administering *less* to others (claim in *Vanda*). Both are "new way[s] of using an existing drug," *Mayo*, 566 U.S. at 87, and "new use[s] of a known process … [or] composition of matter," 35 U.S.C. § 100(b); *see id.* § 101.

Indeed, the claim in *Vanda* preempted a broader range of activity than Mallinckrodt's. It claimed *all* doses of 12 mg/day or less, whereas Mallinckrodt's claims cover only a single, specific course of action. The course of action in Mallinckrodt's claims, moreover, was an even greater departure from prior practice. Administering inhaled nitric oxide was the standard of care for most neonatal patients with hypoxic respiratory failure, and no other pulmonary vasodilator was approved for such treatment. Excluding certain patients from treatment with inhaled nitric oxide was thus not inherently the most promising response to the discovery of an adverse effect on a particular patient population. Alternatives to withholding inhaled nitric oxide might have included administering a lower dose to those patients, increasing monitoring for adverse effects, or taking compensatory measures to offset those effects. Mallinckrodt patented only a particular method of selective administration that takes the more extreme step of excluding patients with pre-existing LVD from the inhaled nitric oxide administration—thereby forgoing any benefit from inhaled nitric oxide treatment.

III. THE FEDERAL CIRCUIT'S DECISION THREATENS INNOVATION IN THE NEXT FRONTIER OF MEDICAL RESEARCH—PERSONALIZED MEDICINE

By threatening methods of selective treatment, the decision below disincentivizes the innovation of "refined treatment recommendations" based on "individual patient characteristics." *Mayo*, 566 U.S. at 87. The decision has particularly far-reaching implications for personalized or precision medicine, including the common practice of integrating a companion diagnostic into a treatment protocol to realize the benefits of selective treatment.

Personalized medicine seeks to tailor treatment based on characteristics that make a patient susceptible to certain drugs, or less likely to suffer adverse effects from those drugs. *See* Vogenberg et al., *Personalized Medicine Part I: Evolution and Development into Theranostics*, 35 P&T 560, 560 (2010), https://bit.ly/2oC1uGF. Investment in developing precision treatments is critical to optimizing patient outcomes and avoiding unnecessary medical expense.

As of January 2017, there were 30 approved companion diagnostic assays in the United States. *See* Scheerens et al., *Current Status of Companion and Complementary Diagnostics*, 10 Clin. Transl. Sci. 84, 87-88 tbl. 2 (2017). More than one of every three drugs the FDA approved from 2017 to 2018 was a personalized or precision medicine. *Personalized Medicine at FDA: A Progress & Outlook Report* 4-5, Personalized Medicine Coalition (2018), https://bit.ly/2VzFeM9. In 2018 alone, FDA approved 25 personalized medicines, representing 42% of all drug approvals that year. *Id.*

The decision below creates substantial uncertainty for a large number of patents that protect and reward

those personalized treatments. *See, e.g.*, U.S. Pat. No. 10,208,130 (method of treating gastric cancer based on HER2 protein expression in tumor tissue); U.S. Pat. No. 9,588,122 (method of treating cancer based on expression of protein biomarker); U.S. Pat. No. 8,759,302 (method of selectively treating multiple sclerosis patients based on serum biomarker concentration); U.S. Pat. No. 9,535,075 (method of selectively treating transplant recipients based on expression levels of certain genes); U.S. Pat. No. 8,329,647 (method of selectively treating metabolic syndrome based on biomarkers of insulin resistance and/or pancreatic β-cell dysfunction).

A strong, stable patent system is necessary to encourage private investment in, and public disclosure of, such inventions. The Court should intervene now before the Federal Circuit's erroneous application of judicial exceptions to Section 101 upends the field of personalized medicine.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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