No. 22-1066

In the Supreme Court of the United States

CAREDX, INC., *et al.*,
Petitioners,
v.
NATERA, INC., *et al.*,
Respondents.

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

BRIEF OF RESPONDENT NATERA, INC. IN OPPOSITION

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QUESTION PRESENTED

This Court has long held that "laws of nature, natural phenomena, or abstract ideas" are not patentable under Section 101 of the Patent Act, 35 U.S.C. § 101. *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66, 70-71 (2012); *see also, e.g.*, *O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 112-20 (1854); *LeRoy v. Tatham*, 55 U.S. (14 How.) 156, 175 (1853). Applying that principle in *Mayo*, this Court held that Section 101 prohibits patents claiming processes that "focus[ ] upon the use of a natural law," where the "steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field." 566 U.S. at 72-73.

The question presented is whether the Federal Circuit properly applied *Mayo* in concluding that the patent claims at issue are ineligible under Section 101 because they are directed to detecting an admittedly-natural phenomenon (the presence of an organ donor's cell-free DNA in a transplant recipient's blood, which indicates organ rejection) using measurement techniques that the patents repeatedly admit are "conventional" and "known in the art." Pet. App. 32a-33a & n.5 (citations omitted).

CORPORATE DISCLOSURE STATEMENT

Pursuant to Supreme Court Rule 29.6, respondent Natera, Inc. states that it has no parent corporation and that no publicly held company owns ten percent or more of its stock.

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INTRODUCTION

The patents at issue in this case, similar to those in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), claim methods for detecting naturally-occurring DNA in a person's blood using techniques that the patents themselves describe as conventional or well known in the art. The Federal Circuit correctly applied this Court's precedents and found that these claims are not patentable under Section 101 of the Patent Act, 35 U.S.C. § 101. As the Federal Circuit explained (Pet. App. 16a), the methods claimed by these patents "are indistinguishable from other diagnostic method claims" that this Court found ineligible in *Mayo*.

In *Mayo*, this Court reiterated the longstanding principle that Section 101 "contains an important implicit exception" for "[l]aws of nature, natural phenomena, and abstract ideas." 566 U.S. at 70 (citation omitted). Applying that exception, this Court held that certain medical diagnostic claims were ineligible because they "focused upon the use of a natural law" (a correlation between measurable metabolites and health risks) and the "steps in the claimed processes (apart from the natural laws themselves) involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Id.* at 72-73.

The same is true here. As in *Mayo*, the "practice of the asserted method claims does not result in an inventive concept that transforms . . . natural phenomena into a patentable invention." Pet. App. 20a. The Federal Circuit's fact-bound application of *Mayo* was correct and consistent with other applications of *Mayo* that this Court has declined to

review. *See, e.g.*, *Athena Diagnostics, Inc. v. Mayo Collaborative Services LLC,* 915 F.3d 743 (2019), *cert. denied*, 140 S. Ct. 855 (2020).

Petitioners say little about *Mayo* or the Federal Circuit's application of *Mayo* in this case. The main focus of their petition is a vague insistence (at 10) that this Court "needs to take another Section 101 case." And petitioners assert (at 11) that this case is a good vehicle because it "involves applying the natural-phenomenon exception to medical diagnostics, the field where the need for this Court's review is most pressing." Yet this Court already applied Section 101 in this context in *Mayo*. Petitioners never suggest what is wrong with *Mayo* or how the legal test set out in *Mayo* should be clarified. Instead, they argue (at 21) that the Court should use this case to "focus on the text" of Section 101 by holding that Section 101 allows for patents claiming "an 'improvement' upon prior useful methods for measuring a particular natural phenomenon." *Mayo* already provides for that result in appropriate cases. Furthermore, this Court has repeatedly and recently rejected other petitions calling for review of these issues in cases involving similar diagnostic patents, such as *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 140 S. Ct. 855 (2020).

Even if this Court were inclined to revisit *Mayo*, this petition is not a suitable vehicle. As petitioners themselves point out, there are plenty of Section 101 cases that have sharply divided judges on the Federal Circuit and generated calls for certiorari. This case is not among them: the panel below decided this case unanimously and with evident ease. When petitioners sought rehearing en banc, the Federal Circuit denied their petition without a single dissent.

Nor have there been widespread calls for further review. Indeed, only one *amicus* brief has been filed in support of certiorari. As that lack of interest suggests, this is not a close case. This case—a straightforward application of *Mayo* that presents nothing new—does not warrant certiorari.

The petition should be denied.

STATEMENT OF THE CASE

A. Section 101 And *Mayo*

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. This statutory language—almost identical to that which Thomas Jefferson drafted for the Patent Act of 1793—has defined the proper subject matter of patents for 230 years. *See Diamond v. Diehr*, 450 U.S. 175, 182-84 (1981) (explaining that Congress's replacement of "art" with "process" in 1952 did not change meaning).

This Court has consistently recognized "an important implicit exception" to this provision. *Mayo*, 566 U.S. at 70. "Laws of nature, natural phenomena, and abstract ideas are not patentable." *Id.* (quoting *Diehr*, 450 U.S. at 185). As the Court explained long ago, "[a] principle, in the abstract, is a fundamental truth; an original cause; a motive; these cannot be patented." *LeRoy v. Tatham*, 55 U.S. (14 How.) 156, 175 (1853). The same is true of "power[s] in nature," which are "open to all." *Id.*

Underlying this rule is a concern that the recognition of exclusive property rights in natural laws, natural phenomena, or abstract ideas will

inevitably hinder innovation. *See Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014). So, for example, when Samuel Morse—having invented the telegraph—claimed a broad, exclusive right to "the use of the motive power of the electric or galvanic current, which [he] call[ed] electro-magnetism, however developed for marking or printing intelligible characters . . . at any distances," this Court rejected that claim as unpatentable. *O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 112 (1854). As the Court explained, "[f]or aught we now know some future inventor, in the onward march of science, may discover a mode of writing or printing at a distance by means of the electric or galvanic current, without using any part of the process or combination" disclosed by Morse. *Id.* at 113. "[Y]et if it is covered by this patent the inventor could not use it, nor the public have the benefit of it without [Morse's] permission." *Id.* The Court recognized that permitting Morse's claim would "shut[ ] the door against inventions of other persons." *Id.* It was therefore "not warranted by law." *Id.*

That principle prevailed through the twentieth century. In *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948), this Court addressed patent claims for a mixed culture of rhizobia—bacteria that fix nitrogen when attached to the roots of legumes. As the Court explained, it had "long been well known" how to "produc[e] a bacterial culture" that would effectively inoculate the seeds of legumes with rhizobia so that the legumes could fix nitrogen. *Id.* at 129. Yet because different species of rhizobia attach to the roots of different species of legumes, the existing practice was to "manufacture and sell inoculants containing only one species of root-nodule

bacteria," such that "if a farmer had crops of clover, alfalfa, and soy beans he would have to use three separate inoculants." *Id.* A patentee discovered "strains of each species of root-nodule bacteria which do not exert a mutually inhibitive effect on each other," and found that those bacterial strains could, "by certain methods of selection and testing, be isolated and used in mixed cultures." *Id.* at 130. He thus sought to claim "a mixed culture of Rhizobia capable of inoculating the seeds of" a wide variety of legumes. *Id.*

The Court found such claims unpatentable. As it explained, while the patentee's mixed culture reflected "an important commercial advance," the only act of discovery involved in his mixed culture was "the discovery of [a] natural principle." *Id.* at 132. The patentee discovered that "each species of these bacteria can be mixed without harmful effects to the properties of either," which was simply a discovery of the "qualities of non-inhibition" of the bacteria. *Id.* at 131. "The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement in the range of their utility." *Id.* Discovery of the "qualities of these bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none." *Id.* at 130.

The Court applied that principle again in *Parker v. Flook*, 437 U.S. 584 (1978), a case involving patent claims for "alarm limits" used in the catalytic chemical conversion of hydrocarbons. As the Court recognized, the only purportedly inventive or novel aspect of the patentee's claims was the application of a new algorithm for calculating such alarm limits;

everything else recited in the patent claims was "well known" in the prior art. *Id.* at 594-95. But such "algorithm, or mathematical formula, is like a law of nature," *id.* at 589, in that it "reveals a relationship that has always existed," *id.* at 593 n.15. Accordingly, "once that algorithm is assumed to be within the prior art, the application, considered as a whole, contains no patentable invention." *Id.* at 594. In other words, the discovery of a "phenomenon of nature or mathematical formula . . . cannot support a patent unless there is some other inventive concept in its application." *Id.* As the Court elsewhere summarized this trail of precedents, the "laws of nature, physical phenomena, and abstract ideas . . . [are] not patentable." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980).

This Court unanimously brought that rule to bear in *Mayo*. *Mayo* concerned "patent claims covering processes that help doctors who use thiopurine drugs to treat patients with autoimmune diseases determine whether a given dosage is too low or too high." 566 U.S. at 72. As the Court explained, the patents rested on existing scientific findings that "the levels in a patient's blood of certain metabolites . . . were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective." *Id.* at 73-74. But scientists "did not know the precise correlations between metabolite levels and likely harm or ineffectiveness." *Id.* at 74. The patent claims at issue in *Mayo* "set forth processes embodying researchers' findings that identified these correlations with some precision." *Id.*

The Court held that these process claims were ineligible for patenting under Section 101. As the Court explained, the "process that each claim recites

tells doctors interested in the subject about the correlations that the researchers discovered." *Id.* at 78. Those correlations are "a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes." *Id.* at 77. So the patents' description of those precise correlations did nothing more than "set[ ] forth laws of nature." *Id.* The Court recognized that the claims set forth other process steps in connection with those correlations, and that those "additional steps are not themselves natural laws." *Id.* at 78. Yet it concluded that those "additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." *Id.* at 79-80. Thus, the claims' process steps were "not sufficient to transform unpatentable natural correlations into patentable applications of those regularities." *Id.* at 80.

In reaching that conclusion, this Court unanimously rejected the government's argument as *amicus* 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." *Id.* at 89. In particular, the government had asserted that "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 [a] screening function" for patents that combine discoveries of natural phenomena with non-novel or obvious process steps. *Id.* (final alteration added). As the Court

explained, that argument was "not consistent with prior law" and "would make the 'law of nature' exception to § 101 patentability a dead letter." *Id.* While the Court recognized that its Section 101 analysis entailed some "overlap" with the "novelty inquiry" of Section 102, it explained that "shift[ing] the patent-eligibility inquiry entirely to . . . later sections" of the Patent Act would risk "creating significantly greater legal uncertainty." *Id.* at 90.

Further, the Court rejected the policy argument that mere "research leading to the discovery of laws of nature" warrants patent protection, "particularly in the area of diagnostic research." *Id.* at 91. As the Court acknowledged, "the promise of exclusive rights provides monetary incentives that lead to creation, invention, and discovery." *Id.* at 92. But "that very exclusivity can impede the flow of information that might permit, indeed spur, innovation." *Id.* The Court explained that it would not depart "from established general legal rules lest a new protective rule that seems to suit the needs of one field produce unforeseen results in another." *Id.* It noted that Congress may "craft[ ] more finely tailored rules where necessary." *Id.* The Court thus held that it "need not determine here whether, from a policy perspective, increased protection for discoveries of diagnostic laws of nature is desirable." *Id.*

Finally, this Court unanimously reaffirmed *Mayo* in *Alice*. There, the Court boiled down *Mayo*'s analytical framework into a two-step inquiry. *Alice*, 573 U.S. at 217-18. First, the Court determines "whether the claims at issue are directed to . . . patent-ineligible concepts"—that, is "laws of nature, natural phenomena, [or] abstract ideas." *Id.* at 217. If so, the Court then proceeds to a second step in

which it considers any additional claim elements "both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 79, 78). This second step is designed to test whether the patent claims an "inventive concept" that makes the "patent in practice . . . significantly more than a patent upon the ineligible concept itself." *Id.* at 217-18 (quoting *Mayo*, 566 U.S. at 72-73). *Alice* reaffirmed that, at this second step, the presence of "conventional [process] steps, specified at a high level of generality," is "not enough to supply an inventive concept." *Id.* at 222 (citation omitted).

B. The Patent Claims At Issue

This case concerns three patents owned by Stanford University and exclusively licensed to CareDx, Inc., an organ-transplant diagnostics company: U.S. Patent Nos. 8,703,652 (the '652 patent), 9,845,497 (the '497 patent), and 10,329,607 (the '607 patent). All three patents share the same specification and disclose processes for detecting an organ donor's "cell-free DNA" (cfDNA) in the blood of an organ transplant recipient. Pet. App. 3a.

When an organ is transplanted and rejected by the body of the organ recipient, the organ recipient's natural immune response destroys the cells of the organ donor. These cells contain the organ donor's DNA, which is released upon cellular destruction into the bloodstream of the organ recipient as extracellular, or cell-free DNA. *Id.* Accordingly, detection of elevated levels of an organ donor's cfDNA in the bloodstream of an organ recipient can be used to diagnose organ transplant rejection. *Id.* As

petitioners acknowledge, scientists have known of the "natural correlation" between the presence of an organ donor's cfDNA in the bloodstream of the recipient and the risk of organ transplant rejection for 25 years. Pet. 4.

The patent claims asserted by petitioners recite four steps for detecting an organ donor's cfDNA in the blood of an organ recipient. Pet. App. 8a-9a. The patents' common specification expressly states that the techniques referred to in these steps are, "conventional techniques of immunology, biochemistry, chemistry, molecular biology, microbiology, cell biology, genomics, and recombinant DNA, which are within the skill of the art." *Id.* at 32a-33a (quoting '652 patent). Indeed, the specification is "replete with characterizations of the[se] techniques in terms that confirm their conventionality." *Id.* at 33a.

First, the claims call for obtaining a bodily sample containing cfDNA (e.g., blood or plasma) from the organ recipient. *Id.* at 32a. According to the patents' common specification, this can be done using "any technique known in the art," including by "syringe or other vacuum suction device," confirming that the sample indisputably is a naturally occurring composition. *Id.* at 33a n.5 (quoting specification).

Second, the claims call for "genotyping," i.e., detecting genetic profiles of either the organ donor or the organ recipient, in order to develop a "polymorphism" profile or "SNP" (single nucleotide polymorphism) profile. *Id.* at 32a. Again, polymorphisms are the naturally occurring genetic changes present in the cfDNA, and the common specification makes clear that such genotyping may be performed "using existing genotyping platforms

know[n] in the art." *Id.* at 33a n.5 (alteration in original) (quoting specification).

Third, the claims call for taking the organ recipient's bodily sample and either "sequencing," i.e., determining the naturally existing nucleotide sequence of, the cfDNA in that sample or performing a digital polymerase chain reaction (digital PCR) to detect and differentiate between the organ recipient's and the organ donor's cfDNA based on their genetic differences. *Id.* at 32a. Once again, the common specification confirms that such methods are well known in the art and can be performed using commercially available tools. *See id.* at 33a n.5 (discussing specification's references to, *inter alia*, the use of "high-throughput shotgun sequencing of circulating nucleic acids . . . as well as other methods known in the art" (quoting specification)).

Fourth, the claims call for "determining" or "quantifying" the amount of the organ donor's cfDNA in the sample provided by the organ recipient. *Id.* at 32a. As before, the claims' common specification makes clear that as to this step the claims recite "[m]ethods . . . [that] are known in the art." *Id.* at 33a n.5 (first alteration in original) (quoting specification).

C. Procedural History

Petitioners sued Natera for patent infringement in March 2019, alleging that Natera's kidney transplant rejection test, Prospera, infringed the '652 and '497 patents; petitioners later amended their complaint against Natera to assert the '607 patent. Pet. App. 34a. Petitioners also sued Eurofins Viracor, Inc., alleging that Eurofins's organ transplant rejection tests infringed the '652 patent. *Id.*

Natera and Eurofins moved to dismiss petitioners' complaints on the ground that the asserted claims are unpatentable under Section 101. *Id.* Specifically, respondents argued that the asserted claims are all "directed to a natural phenomenon (i.e., the correlation between transplant rejection and the presence of naturally occurring cfDNA) and therefore are not eligible for patenting." *Id.* at 35a. The district court denied Eurofins's motions to dismiss and Natera subsequently withdrew its motion. *Id.* at 38a. Though it declined to dismiss the suits, the district court directed the parties to proceed to summary judgment on respondents' threshold Section 101 invalidity arguments. *Id.*

The district court ultimately determined at summary judgment that that all of the asserted claims are patent-ineligible under Section 101. *Id.* at 57a. In reaching that conclusion, the district court first set out the analytical framework supplied by this Court's decisions in *Mayo* and *Alice*. It explained that, under *Mayo*, where asserted patent claims are directed to "certain laws of nature," and "any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts," then the claims are unpatentable under Section 101. *Id.* at 44a (citation omitted).

Applying that framework, the district court first recognized that the "parties essentially agree . . . that the asserted claims are directed to detecting a donor's cfDNA in a transplant recipient." *Id.* at 45a. And the district court further recognized that it is "undisputed that donor-specific cfDNA and the correlation donor-specific cfDNA has with organ rejection are natural

phenomena." *Id.* at 46a. Thus, the district court recognized that the "dispositive inquiry" under *Mayo* and *Alice* is "whether the claimed methods of detection are conventional." *Id.* And as to that question, the patents' own "written description that the recited detection methods are conventional ends the matter." *Id.* at 47a.

D. The Federal Circuit's Decision

A unanimous Federal Circuit panel affirmed. Writing for the court, Judge Lourie explained that, in order to "distinguish claims to patent-eligible application of laws of nature and natural phenomena from claims that impermissibly tie up such laws and phenomena, we apply the two-part test set forth by the Supreme Court." Pet. App. 12a. Thus, the court first "examine[s] whether the claims are 'directed to' a law of nature or natural phenomenon." *Id.* (quoting *Alice*, 573 U.S. at 217). If so, then the court "proceed[s] to the second inquiry, where [it] examine[s] whether the limitations of the claim apart from the law of nature or natural phenomenon . . . '"transform the nature of the claim" into a patent-eligible application.'" *Id.* (quoting *Alice*, 573 U.S. at 217).

Applying the two-step inquiry prescribed by *Alice* and *Mayo*, the panel concluded that the "claimed methods are indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo* and that [the Federal Circuit] found ineligible on multiple occasions." *Id.* at 16a. It rejected petitioners' argument that the district court had disregarded the first step of the *Alice/Mayo* inquiry, noting that the district court "reviewed the claim language" and "concluded that the claims recite

methods for detecting natural phenomena," consistent with the first step of the *Alice/Mayo* inquiry. *Id.* at 17a. The panel also rejected petitioners' argument that "the patents' claims are directed not to natural phenomena, but to improved laboratory techniques." *Id.* at 18a. As the panel noted, petitioners do "not actually claim any improvements in laboratory techniques—rather, . . . the actual claims of the patent merely recite the conventional use of existing techniques to detect naturally occurring cfDNA." *Id.* Thus, the panel upheld the district court's determination that the "patents' asserted claims are directed to natural phenomena." *Id.*

Next, the panel upheld the district court's determination that "the asserted claims add nothing inventive because they merely recite standard, well-known techniques in a logical combination to detect natural phenomena." *Id.* As the panel noted, the Federal Circuit has "repeatedly held that applying standard techniques in a standard way to observe natural phenomena does not provide an inventive concept." *Id.* at 19a. Here, the panel held that the patents' own "specification confirms that the claimed combination of steps . . . was a straightforward, logical, and conventional method for detecting cfDNA previously used in other contexts, including cancer diagnostics and prenatal testing." *Id.* at 20a. The panel thus concluded that, at step two of the *Alice/Mayo* inquiry, "the practice of the asserted method claims does not result in an inventive concept that transforms the natural phenomena into a patentable invention." *Id.* In sum, because the patents' claims "are directed to a natural law together with conventional steps to detect or quantify the

manifestation of that law, they are ineligible under § 101." *Id.* at 21a. The Federal Circuit therefore affirmed the district court's judgment.

Petitioners sought rehearing en banc. The Federal Circuit denied rehearing without recording any dissent from denial. *Id.* at 83a-84a.

REASONS FOR DENYING THE PETITION

This petition arises from a Federal Circuit decision straightforwardly applying settled Supreme Court precedent (*Mayo*) to the patents at issue. Petitioners' argument ultimately reduces to a call for fact-bound error correction. But there was no error. The Federal Circuit correctly stated the test for patentability set out in *Mayo*. It also correctly recognized that the patent claims at issue here are "indistinguishable" from the patent claims held ineligible in *Mayo* (Pet. App. 16a), and petitioners do not try to argue otherwise. And even though petitioners do not ask this Court to overrule *Mayo*, they assert that this Court should take this case in order to review arguments that this Court rejected in *Mayo*. This Court should decline petitioners' invitation to revisit points of law it already decided in *Mayo*. Finally, even if this Court wishes to revisit *Mayo*, this petition presents a particularly inapt vehicle for doing so. Unlike in other Section 101 cases, the panel's routine application of *Mayo* in this case elicited no calls for further review from the en banc Federal Circuit. *See, e.g., Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 927 F.3d 1333 (Fed. Cir. 2019) (per curiam) (generating nearly 84 pages of opinions concurring in, and dissenting from denial of en banc review).

The petition should be denied.

I. The Federal Circuit's Application Of *Mayo* Does Not Warrant Review

A. This Case Presents A Straightforward Application Of *Mayo*

1. The Federal Circuit's decision below followed inescapably from this Court's decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012). In *Mayo*, this Court confronted patent claims that "set forth laws of nature—namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of thiopurine drug will prove ineffective or cause harm." *Id.* at 77. As the Court recognized, because that "relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes," a patent that "describes that relation sets forth a natural law." *Id.*

The only remaining question in *Mayo* was whether the patent claims at issue there did "significantly more than simply describe these natural relations," so as to "allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws." *Id.* This Court concluded that they did not because "any additional steps" identified in the patent claims "consist[ed] of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." *Id.* at 79-80. More specifically, the Court recognized that the remaining process steps disclosed in the patents instructed that "the level of the relevant metabolites in the blood" should be determined using "whatever process the doctor or the

laboratory wishes to use," employing "methods for determining metabolite levels [that] were well known in the art." *Id.* at 79. Thus, the patent claims directed a person of ordinary skill in the art "to engage in well-understood, routine, conventional activity previously engaged in by scientists who work in the field." *Id.*

The *Mayo* Court may as well have been describing the patents at issue in this case. As in *Mayo*, the patents at issue here describe a natural correlation between the concentration of certain material in a person's blood (here, cfDNA; in *Mayo*, certain metabolites) and health risks. That is, the patents disclose a relationship between the "quantity of . . . donor [cfDNA]" in the blood of an organ transplant recipient and "transplant rejection, graft dysfunction or organ failure." Pet. App. 4a (emphasis omitted) (quoting '652 patent at col. 27 l. 39-col. 28 l. 40). As in *Mayo*, this correlation is a "consequence" of "natural processes," 566 U.S. at 77—here, the process by which an organ recipient's "natural immune response," reacting to a rejected organ transplant, "destroys the donor cells, thus releasing cfDNA from the donated organ's dying cells into the blood." Pet. App. 3a. Thus, as in *Mayo*, the patents "set[ ] forth a natural law." 566 U.S. at 77.

Next, as in *Mayo*, "any additional steps" identified in the patent claims "consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." *Id.* at 79-80. That much is clear from the patent claims themselves, which expressly describe the additional steps disclosed in those claims as being implemented through "conventional techniques" that are "well

known in the art." Pet. App. 15a & n.1 (citation omitted). As the Federal Circuit recognized, on the face of the patents, each and every "step in the purported invention requires only conventional techniques and commercially available technology." *Id.* at 19a. The first step (i.e., obtaining a bodily sample) may be performed using "any technique known in the art." *Id.* (quoting '652 patent at col. 10 l. 11). The second step (i.e., genotyping) may be carried out using "any suitable method known in the art." *Id.* (quoting '652 patent at col. 20 ll. 31-33). The third step (i.e., sequencing or digital PCR) may be executed "using 'well known' techniques and off-the-shelf tools." *Id.* (quoting '652 patent at col. 15 ll. 6-8). And the fourth and final step (i.e., determining or quantifying the amount of cfDNA) may be done "using methods 'known in the art.'" *Id.* (quoting '652 patent at col. 18 l. 56). And the combination of these steps is itself "conventional," having been "previously used in other contexts, including cancer diagnostics and prenatal testing," to detect cfDNA. *Id.* at 20a. Thus, there is "no genuine dispute that the claimed techniques add nothing inventive to the natural phenomenon being detected." *Id.* at 19a.

The Federal Circuit was therefore entirely correct to say that the claimed methods at issue here are "indistinguishable from other diagnostic method claims the Supreme Court found ineligible in *Mayo*," *id.* at 16a, despite petitioners' attempt to rewrite their claims as "improved measurement methods," *id.* at 12a. Indeed, that proposition is so irrefutable that petitioners do not even try to refute it (and do not so much as acknowledge it) in their petition. Petitioners raise a number of arguments, addressed below, for why the Federal Circuit erred. But their failure to

address the Federal Circuit's core reasoning that this case is squarely governed by *Mayo* is a red flag: petitioners would have this Court take up review of patents that are *undisputedly* "indistinguishable" from patent claims this Court held ineligible for patenting in *Mayo*. *Id.* at 13a.

2. Rather than attempt the forbidding task of distinguishing *Mayo*, petitioners fault the Federal Circuit for purportedly misapplying the *Alice/Mayo* two-step framework. Pet. 24-26. In petitioners' telling, the Federal Circuit erred by making "considerations of 'conventionality' critical at both step two *and* step one" of the *Alice/Mayo* analysis. *Id.* at 25. That argument fails.

As to step two, petitioners' argument (at 26) that the Federal Circuit "improperly imported obviousness considerations into *Alice* step two" mischaracterizes the court's decision. The decision did not incorporate an obviousness analysis; rather, it applied the conventionality analysis prescribed by *Mayo* and *Alice*. As the Federal Circuit explained, invoking its Section 101 precedents, it has "repeatedly held that applying standard techniques in a standard way to observe natural phenomena does not provide an inventive concept" sufficient to satisfy *Alice* step two. Pet. App. 19a (citing *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1377 (Fed. Cir. 2015), *cert. denied*, 579 U.S. 928 (2016); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743, 753-54 (Fed. Cir. 2019), *cert. denied*, 140 S. Ct. 855 (2020); *Roche Molecular Sys., Inc. v. CEPHEID*, 905 F.3d 1363, 1372 (Fed. Cir. 2018)). That analysis tracked the analysis in *Mayo*, which explained that where a patent's claims disclose a natural phenomenon and then disclose "additional steps

consist[ing] of well-understood, routine, conventional activity . . . and those steps, when viewed as a whole, add nothing significant," then the patent's claims are ineligible under Section 101. 566 U.S. at 79-80.

Petitioners' contention (at 26) that this conventionality analysis amounted to an improper importation of "obviousness considerations" at step two is inconsistent with *Mayo*. Indeed, this Court rebuffed the same argument in *Mayo*: it acknowledged that, "in evaluating the significance of additional steps, the § 101 patent-eligibility inquiry . . . might sometimes overlap" with the novelty and obviousness inquiries prescribed by Section 102 and Section 103. 566 U.S. at 90. But this Court recognized that this overlap could not always be avoided without "mak[ing] the 'law of nature' exception to § 101 patentability a dead letter." *Id.* at 89. Again, petitioners simply ignore *Mayo* and fail to explain how the Federal Circuit's analysis is inconsistent with *Mayo*.

Petitioners also contend (at 25) that the Federal Circuit committed "serious analytical error" by discussing conventionality at step one. But in trying to argue that the claims at issue are actually directed to an "*improved* lab technique," Pet. App. 18a (emphasis added), rather than observation of a natural phenomenon, petitioners themselves drew the Federal Circuit's attention to the question of conventionality. The Federal Circuit's step one analysis was correct: it upheld the district court's review of the "claim language," which properly "concluded that the claims recite methods for detecting natural phenomena." *Id.* at 17a. The Federal Circuit then turned to petitioners' argument that the patent claims were directed to "improved

laboratory techniques." *Id.* at 18a. It rejected that argument because the patents do "not actually claim any improvements in laboratory techniques" but instead "merely recite the conventional use of existing techniques to detect naturally occurring cfDNA." *Id.* Petitioners offer no explanation for how the Federal Circuit could have addressed their argument about "improved" techniques *without* addressing conventionality.

3. Petitioners dispute (at 27-30) the merits of the Federal Circuit's conventionality determination, but that fact-bound argument does not warrant this Court's review and does not identify any error. Plaintiffs' conclusory assertions (at 27) that the methods disclosed in the patents are "improved" and "brand new" directly contradict the plain language of the patents' common specification, which unambiguously states that the claimed methods are "'well known in the art'" and may be implemented using commercially available tools. Pet. App. 15a-16a n.1, 18a (citation omitted). Petitioners state (at 28) that they "strongly disagree with the Federal Circuit's understanding of the specification's language," but they do not explain their "strong[ ] disagree[ment]" and it is hard to see how they could possibly do so.

Instead, petitioners pivot (at 29) to the argument that, under this Court's precedents, the claims are "clearly patent eligible" because they "apply the natural phenomenon (the correlation between the proportion of donor cell-free DNA and organ rejection) in a new way." Yet because the Federal Circuit correctly found that the techniques disclosed in the patent claims are not new, Pet. App. 18a-20a, the only sense in which the claims are "new" is that they disclose the application of those well-known

techniques to the natural phenomenon at issue here: namely, observing the levels of an organ donor's cfDNA in an organ transplant recipient's blood.

That is an argument for patentability that this Court has rejected time and again. As the Court put it in *Parker v. Flook*, for example, petitioners "incorrectly assume[ ] that if a process application implements a [natural] principle in some specific fashion, it automatically falls within the patentable subject matter of § 101." 437 U.S. 584, 593 (1978). Here, as in *Flook*, once the natural phenomenon "is assumed to be within the prior art, the application, considered as a whole, contains no patentable invention." *Id.* at 594. As the Federal Circuit recognized, all of the steps disclosed in the patent claims at issue here—including the "claimed combination of steps"—were "previously used in other contexts, including cancer diagnostics and prenatal testing." Pet. App. 20a.

It cannot be the case that simply shifting a combination of known techniques from the investigation of one natural phenomenon to the investigation of another natural phenomenon results in a patentable invention. A scientist who tries to claim methods for observing a novel form of cell division using microscopic tools that are known in the art does not claim anything new other than the natural phenomenon she is observing. "[S]imply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Mayo*, 566 U.S. at 82. The Federal Circuit's routine application of that principle in this case does not warrant review.

B. There Is No Reason To Revisit *Mayo*

All of the foregoing is enough to dispose of the petition. This case is governed by—and correctly decided under—*Mayo*. And since petitioners do not ask this Court to overrule *Mayo*, their petition should be denied.

Yet while petitioners do not ask this Court to overrule *Mayo*, they advance two arguments suggesting that the Court should revisit the points of law decided in *Mayo*. In particular, petitioners urge this Court to take this case so that it can "return[ ] the focus of the eligibility analysis to Section 101's statutory text." Pet. 20. They also advance broad-gauge policy arguments lamenting the state of Section 101 law, particularly in cases involving "diagnostic method[s], the field where the need for this Court's review is most pressing." *Id.* Those arguments are deeply flawed.

1. Petitioners correctly note that statutory interpretation must always "begin[ ] with the text." *Id.* (quoting *Ross v. Blake*, 578 U.S. 632, 638 (2016)). But while statutory interpretation always begins with the text, it does not always end there. This case concerns a historically well-established and "important implicit exception" to the text of Section 101: specifically, the rule that "[l]aws of nature, natural phenomena, and abstract ideas are not patentable." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 573 U.S. 208, 216 (2014) (citation omitted). This Court has "interpreted § 101 and its predecessors in light of this exception for more than 150 years." *Id.* And, in 1952, Congress effectively ratified that longstanding judicial construction by reenacting the language of Section 101—without substantive

modification—against the backdrop of the implicit exception recognized by this Court. *See* Pub. L. No. 82-593, § 101, 66 Stat. 792, 797 (1952); *Diamond v. Diehr*, 450 U.S. 175, 182-84 (1981); *cf. Ysleta Del Sur Pueblo v. Texas*, 142 S. Ct. 1929, 1940 (2022) ("This Court generally assumes that, when Congress enacts statutes, it is aware of this Court's relevant precedents.").

Petitioners acknowledge that this Court "has characterized its jurisprudence" in this area as "an exception to [the] terms" of Section 101. Pet. 21. They nevertheless argue that this case provides an "opportunity to focus on the text," *id.*, of Section 101's provision for the patenting of "new and useful *improvement[s]*," *id.* (quoting 35 U.S.C. § 101). In petitioners' view, that clause "provides a clear textually-grounded answer in a natural-phenomenon case" like this one. *Id.*

But as discussed at length, petitioners have no evidence that the patent claims at issue in this case improved anything at all. Moreover, petitioners' argument incongruously asks the Court to construe an "implicit" exception, *Alice*, 574 U.S. at 216, in light of explicit statutory text. And petitioners' insistence that such implicit exception be variably applied with respect to different clauses of that text makes even less sense: petitioners' only textual justification for this notion is that "an 'improvement' necessarily does not claim a natural phenomenon" because "[n]atural phenomena are preexisting and cannot be improved upon while still remaining natural." Pet. 21. Yet it is also the case that a patent claiming any "*new* and useful process, machine, manufacture, or composition of matter," 35 U.S.C. § 101 (emphasis added), will not directly claim a natural phenomenon, since—as

petitioners themselves note—natural phenomena are "preexisting." *See, e.g.*, *Diamond v. Chakrabarty*, 447 U.S. 303, 309-10 (1980) (explaining that a synthetic bacterium qualified as patentable subject matter under Section 101 because it was "not . . . a hitherto unknown natural phenomenon," but rather "a *new* bacterium with markedly different characteristics from any found in nature" (emphasis added)). Petitioners' emphasis on the text is therefore misplaced.[1]

Moreover, this Court's precedents make clear that the fact that a patented product or method is described as an "improvement" over existing products or methods does not, in and of itself, take such claim outside the scope of the exception for claims directed to natural laws, natural phenomena, and abstract ideas. In *Funk Brothers Seed Company*, for example, the patent owner characterized the patent claims at issue—reciting a new mixed culture of bacteria—as claims directed at an "improvement." Respondent Br. 15, 17, *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) (No. 280), 1948 WL 47563. And it *was* an improvement, at least in a colloquial sense: as the Court noted, the patent owner's mixed culture "may well have been an important commercial advance." *Funk Bros. Seed Co.*, 333 U.S. at 132; *see id.* at 131 ("There is, of course, an advantage in the combination."). But this was not enough to state a claim for "invention within the meaning of the patent statutes," since the advance flowed from "the

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[1] And, as explained above, petitioners' arguments are doubly misplaced here in light of petitioners' failure to show any actual improvements their patents have made to a laboratory technique or practice. *See supra* at 17-18.

discovery of some of the handiwork of nature." *Id.* As the Federal Circuit put it in this case, a claim like that "add[s] nothing inventive to the natural phenomenon being detected." Pet. App. 19a.

In any case, petitioners' argument here does not present any reason for this Court to revisit its decision in *Mayo*. The *Mayo* framework *already* provides for the patentability of claims that disclose improvements over existing methods—even if those claims are also directed at natural phenomena. That is, under *Mayo*, a patent claim directed at a natural phenomenon may still be eligible for patenting so long as it discloses additional, "unconventional steps" that "confine[ ] the claim to a particular, useful application" of the natural phenomenon. 566 U.S. at 84. That rule protects patent claims that disclose "the kind of 'discoveries' that the [Patent Act] was enacted to protect" while barring patent claims whose "inventive concept" rests solely on the natural phenomenon itself. *Flook*, 437 U.S. at 593-94. Once again, petitioners' arguments simply ignore *Mayo* and the precedents upon which *Mayo* rests.

2. Petitioners also portray this Court's Section 101 jurisprudence as having fostered a policy crisis. They argue broadly that this Court must take a Section 101 case because the Federal Circuit is "at a loss as to how to uniformly apply § 101," Pet. 15 (quoting *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, 977 F.3d 1379, 1382 (Fed. Cir. 2020) (Moore, J., concurring)), and the "practical impact of the uncertainty is severe," *id.* at 17. The uncertainty is so severe, petitioners assert, that it has "reduced investment in new technologies" and "driven industry to foreign jurisdictions." *Id.* (citation omitted). In petitioners' view, only this Court's further "guidance

on the correct application of Section 101" can stem an inexorable drain of "critical life sciences and information technology inventions" to the likes of "the People's Republic of China" and "Europe." *Id.* (citation omitted).

That argument falls flat. As noted in *Alice*, for over 150 years this Court has been applying roughly the same "implicit exception" to Section 101 for "[l]aws of nature, natural phenomena, and abstract ideas." 573 U.S. at 216. Throughout, the United States has been the undisputed global leader in scientific innovation and industrial application of scientific breakthroughs. *See generally* National Academies of Sciences, Engineering, & Medicine, *Protecting U.S. Technological Advantage* (2022), https://nap.nationalacademies.org/catalog/26647/protecting-us-technological-advantage. That remains true today, including and perhaps most especially in the life sciences and in information technology. *See, e.g.*, Beethika Khan et al., National Science Board, *Science and Engineering Indicators: The State of U.S. Science and Engineering* at 13 (Fig. 24) (2020), https://ncses.nsf.gov/pubs/nsb20201 (showing that, in 2018, the United States accounted for 32% of value-added global output in R&D-intensive industries, such as pharmaceuticals and software publishing).

This Court's Section 101 jurisprudence has an important role to play in American innovation. As this Court has recognized repeatedly, "[l]aws of nature, natural phenomena and abstract ideas" are "the basic tools of scientific and technological work," *Mayo*, 566 U.S. at 70-71 (first quoting *Diehr*, 450 U.S. at 185; then quoting *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)), and allowing patentees to monopolize natural phenomena and abstract ideas "might tend to

impede innovation more than it would tend to promote it," *id.* at 71. While application of the law-of-nature exception in the field of medical diagnostics has generated some controversy, that controversy is nothing new. This Court heard from numerous *amici* on both sides of this issue in *Mayo*. But this Court ultimately recognized that specific policy concerns about Section 101 patentability with respect to medical diagnostics are best addressed to Congress, not this Court. "[P]atent law's general rules must govern inventive activity in many different fields of human endeavor . . . ." *Id.* at 92. This Court should accordingly "hesitate before departing from established general legal rules lest a new protective rule that seems to suit the needs of one field produce unforeseen results in another." *Id.* The job of "crafting more finely tailored rules where necessary" belongs to "Congress." *Id.*; *cf.* Patent Eligibility Restoration Act of 2023, S. 2140, 118th Cong. § 3(a)(2) (2023) (proposing to amend Section 101 in substantial part). Petitioners' policy arguments should prove no more persuasive to this Court than they proved 11 years ago in *Mayo*.

3. It is worth noting, too, that this Court has had no shortage of opportunities to revisit Section 101 and *Mayo* in recent years, including in several cases involving medical diagnostics; it has declined them all. *See, e.g.*, *Tropp v. Travel Sentry, Inc.*, 143 S. Ct. 2483 (2023); *Interactive Wearables, LLC v. Polar Electro Oy*, 143 S. Ct. 2482 (2023); *Universal Secure Registry LLC v. Apple Inc.*, 142 S. Ct. 2707 (2022); *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, 142 S. Ct. 2902 (2022); *Trading Techs. Int'l, Inc. v. IBG LLC*, 140 S. Ct. 954 (2020); *HP Inc. v. Berkheimer*, 140 S. Ct. 911 (2020); *Hikma Pharms. USA Inc. v.*

Vanda Pharms. Inc., 140 S. Ct. 911 (2020); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 140 S. Ct. 855 (2020) (medical diagnostics); *TS Patents LLC v. Yahoo! Inc.*, 139 S. Ct. 1569 (2019); *Sequenom, Inc. v. Ariosa Diagnostics, Inc.*, 579 U.S. 928 (2016) (medical diagnostics).

Indeed, the Court rejected these petitions even though the government recommended granting several of them. *See* United States Amicus Br. 23, *Interactive Wearables, LLC v. Polar Electro Oy*, 143 S. Ct. 2482 (2023) (Nos. 21-1281, 22-22), 2023 WL 2817859; United States Amicus Br. 22, *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, 142 S. Ct. 2902 (2022) (No. 20-891), 2022 WL 1670811.

This petition not only calls for fact-bound error correction; it also raises the same issues presented by many other recent petitions. This Court denied all of those petitions. It should deny this one, too.

C. In Any Event, This Case Would Be A Poor Vehicle For Revisiting *Mayo*

Finally, even if this Court were inclined to grant a petition addressing Section 101 and *Mayo*, this case is the wrong vehicle. As explained above, this case is a routine application of *Mayo*, which is why it generated a short, unanimous opinion from the panel, and why petitioners' request for en banc review in the Federal Circuit was denied without a single dissent. Even now, petitioners' request for further review has garnered only a single *amicus* brief—a striking and telling contrast from other Section 101 cases. Certain features of this case—particularly the patents' clear statement that all of the claimed steps have long been known in the art—made resolution of this case straightforward.

If this Court is going to devote its resources to a Section 101 case, it should do so in a *close* Section 101 case—one that has divided the judges of the Federal Circuit, and which has thus raised substantial doubt as to the proper rule or application of law. Such cases crop up on a regular basis, including in the medical-diagnostic context. *See, e.g.*, *Athena Diagnostics*, 927 F.3d 1333 (recording *eight* separate opinions in connection with denial of petition for rehearing en banc in a medical-diagnostic case); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 809 F.3d 1282 (Fed. Cir. 2015) (generating three separate opinions in connection with denial of petition for rehearing en banc in a medical-diagnostic case). This is not one of those cases and, thus, is an especially unpromising candidate for certiorari.

Finally, petitioners (at 30-31) request in the alternative that this Court hold their petition pending the outcomes of *Tropp* and *Interactive Wearables*. As discussed, this Court recently denied certiorari in both cases. Petitioners' request for alternative relief is therefore moot.

CONCLUSION

The petition for a writ of certiorari should be denied.

Respectfully submitted,

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