No. 15-1182

IN THE

Supreme Court of the United States

SEQUENOM, INC.,

Petitioner,

v.

ARIOSA DIAGNOSTICS, INC., NATERA, INC. AND DNA DIAGNOSTICS CENTER, INC.,

Respondents.

On Petition for a Writ of Certiorari
to the United States Court of Appeals
for the Federal Circuit

PETITIONER'S REPLY BRIEF

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Twenty-two separate *amicus* briefs have joined Sequenom's petition in imploring this Court to grant certiorari. That is unprecedented, particularly in a commercial case. Nor are these *amici* merely self-interested advocates for broader patent eligibility, as respondents suggest. Instead, their ranks include diverse patent-law academics, respected organizations of patent-law practitioners representing clients with widely varying interests, well-known companies in multiple scientific fields that are regularly both patent plaintiffs *and* defendants, and foreign patent-law experts. Their depth of patent-law and Supreme Court experience makes these *amici* keenly aware of the pressing patent-law questions that most need this Court's review, and the cases that ideally present them. And, together with multiple disinterested judges, they aver that the question presented needs an answer here to dispel lower-court confusion and avert an incipient "crisis of patent law and medical innovation." Pet.App. 78a (Lourie. J.).[1]

Four critical themes course through both the petition and these *amicus* briefs:

First, this Court has yet to decide this issue—as demonstrated by Judge Linn's careful explanation that "Sequenom's invention is nothing like the invention at issue in *Mayo*," Pet.App. 24a.

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[1] Many are declared enemies of broader patent eligibility. *See, e.g.*, Microsoft Br., *Alice Corp. v. CLS Bank*, No. 13-298 (supporting ineligibility determination in *Alice*). Strikingly, one *amicus* (Novartis) even supports this petition despite holding a huge stake in *one of the respondents*. *See* Ariosa BIO ii; http://goo.gl/9Sedb7.

Second, only this Court can resolve it, as the Federal Circuit's reading of this Court's precedents now sweepingly disqualifies a wide swath of inventions from eligibility, *e.g.*, Novartis Br. 8-20.

Third, the question presented is vitally important for innovation in fields including (but by no means limited to) cutting-edge medical science, *e.g.*, *id.* 22; Amarantus Br. 9.

Fourth, this is an ideal vehicle for the question presented, both because of the manner of its presentation and because the staggering breadth of the ruling below may prevent further good vehicles from arising in the future, *e.g.*, BIO/PhRMA Br. 20-26.

These cert-stage considerations so plainly favor review that respondents can contest only the first with any real seriousness. The essence of their opposition is that this Court has already decided the question presented, and "would have to be prepared to revisit and overrule *Mayo*" in order to grant certiorari. Natera BIO 5; *see* Ariosa BIO 1. But that is obviously false. The language that respondents identify in *Mayo Collaborative Svc. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012), does not approach actually deciding the question presented. At most, they have selected one reading of that decision among several, including another that would both recognize the validity of petitioner's breakthrough invention and avoid endangering so much genuine innovation.

Here is the nub of the dispute: Petitioner's patent teaches how to identify and make effective use of a natural phenomenon discovered by the inventors (cell-free fetal DNA) by implementing three key steps: (1) fractionating maternal blood; (2) amplifying the cell-

free DNA in the plasma portion; and (3) distinguishing cell-free *fetal* DNA from confounding, cell-free *maternal* DNA by searching for identifiably paternal sequences. All agree that the core process tools (amplification and fractionation) were previously known. But it is just as clear that those tools were never previously practiced *in the combination* that the patent directs. Indeed, not only was the patent's combination of these steps unconventional, it was the *opposite* of convention: The well-accepted practice among those searching for non-invasive sources of fetal DNA was to discard the very material the patent teaches them to keep. Thus, the express premise of the Federal Circuit's decision was that Sequenom's invention "combined and utilized man-made tools of biotechnology *in a new way* that revolutionized prenatal care." Pet.App. 18a (emphasis added). Tellingly, while this critical language from the ruling below appears multiple times in the petition—*including the question presented*—neither respondent mentions it once.

The Federal Circuit nonetheless held that all such patents are invalid as a matter of law. The critical step in its reasoning was the holding that, "[f]or process claims that encompass natural phenomenon, the process steps are the additional features that must be new and useful," *id*., meaning that a novel, patentable *step* is always required, even if the inventor is recombining man-made tools in a novel way. Here, because fractionating blood, amplifying DNA, and identifying particular sequences were generally known techniques, the invention was deemed patent-ineligible. It made no difference that the known practice was previously to fractionate maternal blood

in order to discard maternal plasma, nor that the identification of paternal sequences was used as the solution to a maternal-background problem that did not even exist before the inventors (alone) discovered cell-free fetal DNA. *See* Pet. 24.

Notably, the Federal Circuit derived that critical reasoning not from *Mayo* or any other modern case, but from a single inapposite sentence in *Parker v. Flook*, 437 U.S. 584, 591 (1978), on which not even respondents materially rely: "The process itself, not merely the mathematical algorithm, must be new and useful." Not only did *Parker* involve a different question, petitioner's argument is not that "*merely*" the discovery of the natural phenomenon (cell-free fetal DNA) is itself patentable. Instead, the patentable invention is the new combination of physical steps in the process motivated by that path-breaking discovery.

The Federal Circuit's reliance elsewhere on isolated language in *Mayo* caused it to miss how this distinction makes this case utterly different. In *Mayo*, all the process steps were already used in exactly the same combination claimed by the patent: Doctors were already "administering the drug at issue, measuring metabolite levels, and adjusting dosage based on the[m]." Pet.App. 22a (Linn, J.). The only thing the patent added was the discovery of the metabolite's ideal target levels—*i.e.*, raw knowledge of the natural law itself. In contrast, this patent teaches practitioners a *new* combination of physical steps they were not previously practicing together. And so, as the petition explained, this case will allow "the Court [to] brighten the line between a method that merely adds a new discovery to what practitioners were already doing, *see Mayo*, 132 S. Ct. at 1299, and one that, by

the Federal Circuit's own description, 'combine[s] … man-made tools … in a new way' to achieve a revolutionary result." Pet. 12 (quoting Pet.App. 18a).

The Federal Circuit's decision also failed to heed *Mayo*'s own warning against swallowing all of patent law—a concern respondents cannot allay. Particularly in the life sciences, a vast number of previously unimpeachable inventions involve nothing more than new combinations of existing materials and techniques motivated by discoveries about the natural world. The Nobel-winning invention of PCR is only one example. *See* Pet. 14, 28-29. So is every vaccine derived from a natural virus or protein. *Id.* 27-28. Indeed, as the petition explains (at 25-26) and countless *amici* reinforce, *see, e.g.*, Br. of 19 Law Professors 6-10; Microsoft Br. 15-16; Br. of Profs. Lefstin and Menell 9-10, *all* core scientific progress involves using an insight about the natural world to motivate new combinations of the tools and materials inventors find around them, so that excluding such inventions would mean that everything from the light bulb to the Nation's first patented process deserves no patent-law protection at all. Accordingly, respondents do not even contest that the Federal Circuit's rule will throw into doubt both the settled expectations on which hundreds of billions in life-sciences research have been invested, and the incentive structure that supports future innovation in the field. Nor is the problem limited to life sciences: Respondents lack a theory of scientific progress that would save patents in *any* field.

Respondents' only answer is to say—in *Mayo*'s words and without elaboration—that "those inventions 'add *enough* to their statements of the [natural law or phenomenon] to allow the processes they describe to

qualify as patent-eligible processes that *apply* natural laws.'" Ariosa BIO 35 (quoting 132 S. Ct. at 1297) (emphasis added). But, frankly, neither we nor learned *amici* nor the lower courts have any idea what that means.[2] All this language does is state a question; it does not chart an answer in the form of any legal rule that courts can consistently apply in any field of invention. What is "*enough*"? Why is PCR "*enough*" and petitioner's invention not? How can "combin[ing] … man-made tools … in a new way" with revolutionary results not be "*enough*," and what other indicia of invention could we possibly use? In short, respondents disclose no concept of "invention" or "inventiveness" that *anyone* in the system could use in determining what qualifies as an "inventive concept." *Mayo*, 132 S. Ct. at 1299.

In truth, it is inconceivable that—as respondents suggest—this Court really intended respondents' favorite clippings from *Mayo* to forever cement an inflexible legal rule, rather than to create a *standard* open to further elaboration through cases just like this one. That is especially true because *Mayo*'s own author has indicated the exact opposite. *See* Pet. 11 (quoting Breyer, J.). And that, ultimately, is the most important point for certiorari purposes. Respondents identify language from this Court's recent decisions, like *Mayo*, and say this Court would have to "overrule" it for a grant to be useful. But it cannot be that this

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[2] *See, e.g.*, Microsoft Br. 7-14 (cataloguing "disarray" in lower courts); NYIPLA Br. 17-18 (noting lower courts' unease with the test as applied); Br. of European and Australian Profs. 6 (asking for clarification of test to bring certainty to biomedical sector); BPLA Br. 3 (describing lower courts' confusion over the test).

Court's language in *Mayo* was intended to trigger the Federal Circuit's sweeping holding below—without any briefing on the question or analysis in future cases—simply because *Mayo* adopted a standard under which eligible patent claims must add "*enough*," or supply an undefined "inventive concept."

Indeed, the bid to paint this case as one that seeks to "overrule" *Mayo* is transparently wrong. *Mayo* is obviously the "easy" case, *see id.*, and our system of precedent works by refining the rationales born in easier cases as they face harder tests. Respondents outright ask the Court to ignore judicial intuition and toss genuine inventions like this one out with the bathwater for the sake of unflinching application of "*ex ante* legal standards." Natera BIO 9. But while that may work for a lower court argument, this is the Supreme Court of the United States: Certiorari is the process by which this Court elaborates those very *ex ante* standards. That is precisely why a grant is so essential here.

Likewise, the effort to characterize this case as "*Mayo* redux," *id.* 7, quickly boils down to a simple misstatement of petitioner's argument. *Mayo* clearly holds that adding mere knowledge of a natural law to existing practices is not a patent-eligible inventive contribution. But *Sequenom agrees*, and so does not claim that merely discovering a natural phenomenon (here, cell-free fetal DNA) results in a patent-eligible invention. Instead, the eligible invention is the new combination of physical techniques that the inventors' discovery motivated them to create, apply, and teach to others. The most respondents can fairly say is that they have identified one possible reading of *Mayo* under which such an invention must be condemned

because the inventors' greatest contribution was a discovery about the natural world. But that reading itself conflicts with other parts of *Mayo* (regarding, for example, the patent eligibility of new uses for old drugs), as well as other fact-patterns discussed in cases like *Myriad* and *Diehr*. *See* Pet. 18-21. That only proves that the critical question presented remains open, and so requires this Court's review.

Respondents' reading of *Mayo* also fails to account for other important statements in this Court's modern patent precedents. For example, in response to this Court's clear endorsement in *Myriad* of the view that the discoverer of a new phenomenon should be "in an excellent position to claim applications of that knowledge," *Ass'n for Molecular Pathology v. Myriad*, 133 S. Ct. 2107, 2120 (2013), Natera says (at 20) that this is so because "nobody else even knows about the discovery yet, so the discoverer has a head-start." *See* Ariosa BIO 33 (arguing this advantage gives inventors "a broad canvass with which to work"). But, lacking any concept of "invention," respondents cannot and do not explain how that head start could possibly be useful when the inventor is—under the Federal Circuit's version of *Mayo*—unable to claim any combinations of existing materials and techniques that are motivated by the new discovery, however specific and useful those new combinations may be (like, say, a previously impossible maternal blood test for fetal gender, *see id.* 21). The only patent-eligible inventions under this approach would seem to be purely serendipitous process innovations where the inventor cannot recite a natural law because he doesn't even understand why his process works or improves existing art. *See* Pet. 29-30.

Mayo also endorsed this Court's prior ruling in *Diamond v. Diehr*, 450 U.S. 175 (1981), a decision the panel below did not even attempt to distinguish, and is in fact indistinguishable. *Diehr* expressly holds that "a new combination of steps in a process may be patentable *even though all the constituents* of the combination *were well known and in common use* before the combination was made." *Id.* at 188. *Mayo* unequivocally endorsed the same principle. 132 S. Ct. at 1298 (emphasis added). That principle decides this case in petitioner's favor based on the premises with which the Federal Circuit expressly "agree[d]," Pet.App. 18—namely, that petitioner's combination of existing techniques was "new" and "revolutionary." Neither BIO remotely explains why *Diehr* does not authorize patenting a concededly new combination of techniques that finally enables a long-pursued but previously impossible scientific result. And yet, the now-binding view of the Federal Circuit is that *Mayo* leads to the opposite of *Diehr*'s rule on this point, even though *Mayo* endorsed that very rule by name. That kind of doctrinal confusion cries out for this Court's intervention.

Meanwhile, respondents only deepen that tension by relying on outdated and explicitly rejected theories of patent ineligibility. For example, Ariosa relies heavily (at 24-25) on *Funk Brothers v. Kalo Inoculant Co.*, which suggested that a new product is patent ineligible if, "once nature's secret" regarding the desired qualities of the product is discovered, "the state of the art made the production … a simple step." 333 U.S. 127, 132 (1948). This approach essentially asks courts to consider the patent-ineligible discovery a part of the prior art, and then ask if the patent's

invention would be obvious—much like the Federal Circuit did below. But *that* approach is squarely contrary to the unanimous holding in *Myriad* that cDNA is patent eligible even though it is unquestionably obvious how to make the cDNA that corresponds to a relevant gene once "nature's secret" about that gene is revealed. *See Myriad*, 133 S. Ct. at 2120. Not even respondents know how to reconcile these ideas. *See* Ariosa BIO 34 (relying, later, on patent eligibility of cDNA to deny sweeping effect of decision below). Accordingly, only this Court can now clarify how an "inventive concept" is actually identified, and the extent to which a path-breaking discovery that motivates new combinations of known techniques can, in fact, supply one. *See* Pet.App. 84a (Dyk, J.).

This case is a uniquely perfect vehicle for answering that question not only because of the Federal Circuit's core premise (which respondents entirely ignore), but also because of its unusual preemption fact pattern (which respondents entirely misunderstand). Respondents suggest that Sequenom believes complete preemption is required for patent ineligibility, in the sense that a patent on a natural law or phenomenon would be saved if the claims were arbitrarily limited "to a particular technological environment" or added "insignificant post-solution activity," Natera BIO 24; Ariosa BIO 29-30. But that characterization of Sequenom's position is exactly backwards.

Sequenom of course agrees that complete preemption is not required, and that a patentee cannot save their claims by arbitrarily limiting them to one field or another. What makes this case utterly unique

from the standpoint of preemption analysis, however, is that there are clearly other *solutions* to the *very problem* addressed by the patent, in the patent's *own, specific technological environment*, which the patent concededly does not preempt. Specifically, it has been shown that each of the process steps taught in the patent can be avoided by non-patented methods that still put cffDNA to use in the exact same technological field—*i.e.*, the non-invasive diagnosis of fetal genetic traits. Pet. 5; Ariosa BIO 31. This is miles away from arguing non-preemption when a petrochemical company only claims use of a natural law in petrochemical processing, *see id.* 29 (discussing *Flook*), or a patent claims computer-based hedging in commodities rather than energy markets, *id.* 30 (discussing *Bilski v. Kappos*, 561 U.S. 593 (2010)). Here, *competitors* can concededly use cffDNA through non-patented methods to pursue the same ends pursued by Sequenom's own patented technology, proving that Sequenom necessarily claimed something other than the mere natural phenomenon itself. Respondents do not come close to identifying a previous case with that fact pattern, and this unique aspect of this case counsels strongly in favor of certiorari as well.[3]

Ultimately, there can be no dispute that this case presents the hard question this Court's Section 101

[3] As the petition explains (at 20-21), respondents' endorsement of the district court's time-of-the-patent test for preemption is nonsensical. Among other problems, respondents concede that no one else even knows about the discovery at that time (*see* Natera BIO 20), so it is literally impossible to imagine other proven uses existing at that moment.

jurisprudence has not yet tried to answer. Here, unlike *Mayo*, the inventors did not just add knowledge about the world to existing practices. Instead, the premise of the decision below is that they used what they alone knew about the world to motivate a new combination of pre-existing techniques, enabling revolutionary practical results. *Mayo* surely *asks* if that's "*enough*." This case demands the answer.

CONCLUSION

The petition should be granted.

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