No. 10-1150

In the Supreme Court of the United States

MAYO COLLABORATIVE SERVICES (D/B/A MAYO MEDICAL LABORATORIES) AND MAYO CLINIC ROCHESTER,
Petitioners,

v.

PROMETHEUS LABORATORIES, INC.,
Respondent.

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

REPLY BRIEF FOR PETITIONERS

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Prometheus concedes (at 14, 32) that the "proper application of § 101" to medical testing and treatment is "of great importance," with "widespread effects" on "public health" and "multi-billion dollar industries." It concedes too (at 34) that if the Federal Circuit's interpretation is correct, "physicians in the course of patient care" will be "less able to avoid patent infringement than professionals in other fields" because of their "ethical obligations" to patients. Little wonder, then, that the American Medical Association and numerous other medical colleges and associations ("AMA Br."), the American Association of Retired Persons ("AARP Br."), and leading medical laboratories ("Quest Br." in No. 09-490, http://tiny.cc/osfnb) have urged this Court to grant review.

Prometheus acknowledges that its "process" consists merely of administering existing drugs and testing blood for natural metabolites—ordinary medical practice using long-established methods that Prometheus did nothing to advance—followed by consideration of a range of metabolite numbers that suggest a possible dosage change. Opp. 11-12. Prometheus believes it can stop Mayo from administering drugs, testing blood, and then using the knowledge and experience of its own researchers to conclude that Prometheus's metabolite range is *wrong* and that patients are better served by using Mayo's different range. Opp. 24, 28. Incredibly, it claims this monopoly covers *any* autoimmune disease, and asserts that infringement occurs even when a physician *rejects* dosage changes, on the theory that the physician has been warned by, *i.e.* has thought about, Prometheus's numerical ranges. Opp. 24-25. Prometheus points to just one way for physicians to escape this embargo on research and treatment—to *not use blood tests* but

instead develop entirely new ways to measure metabolite levels. Opp. 27.

The AMA describes as "profound" and "unthinkable" the practical consequences of the Federal Circuit's decision: it will "slow the development of diagnostic testing," "undermine competition to provide inexpensive and high-quality testing," and lead "to higher-priced medical treatment." AMA Br. 12-14. It was not the "intent of Congress" in Section 101 that "a process claim" should "confer power to block off whole areas of scientific development" by creating a "monopoly of knowledge." *Brenner*, 383 U.S. at 532, 534. The need for this Court's review is urgent.

1. Prometheus's contention (at 16) that this dispute centers on "claim construction" rests on empty wordplay. There is no dispute as to the nature of Prometheus's claims—as this Court recognized when it rejected precisely the same argument by vacating and remanding in response to Mayo's first certiorari petition. Prometheus's claims—the Federal Circuit, Prometheus, and Mayo agree—consist either of the three steps of administering a drug, determining metabolite levels produced by the body in biologic reaction to the drug, and then positing a metabolite range that "indicates a need" to consider changing dosage (*e.g.*, Claim 1, Pet. App. 4a), or the last two steps only (Claim 46, Pet. App. 5a). As Prometheus successfully argued in the district court, the final step does not require treatment but is satisfied when the physician or researcher is "warned" or "notified" that a dosage adjustment *may* be indicated. Pet. App. 108a-109a. The Federal Circuit reached the same conclusion. Pet. App. 23a (result is "useful information for possible dosage adjustments").

"Administering" and "determining" are not "concrete steps that confine the patent's scope." Opp. 12. They impose no limit because the final mental step—the only one to which Prometheus made any contribution—preempts all relevant uses of "naturally occurring" correlations between drugs and metabolite levels. Pet. App. 15a. Prometheus concedes as much when it says that Mayo cannot develop a better and cheaper test with different criteria relating to *any* autoimmune disease unless it invents (needlessly) an entirely new way of examining the body for metabolites. Opp. 25, 27. It does so again when it acknowledges that a physician cannot even decide *not* to use Prometheus's correlations without buying a license. Opp. 24. The broad scope of the patent is confirmed by testimony of Prometheus's expert that a physician who receives test results referring to these metabolite ranges infringes regardless whether she "crumples it up, throws it away, reads it, acts on it, doesn't act on it, any assumptions you want to come up with." Pet. 22.

Prometheus downplays its attack on Mayo researcher Dr. el-Azhary with the assertion that it "does not sue doctors." Opp. 24. But it deposed Dr. el-Azhary—who was engaged in research, *not* treatment—and made a centerpiece of its argument that she infringed Prometheus's patents when she administered drugs to dermatology patients, tested their blood for metabolites, and investigated the optimal therapeutic range for dermatology patients, because Prometheus's patents monopolize the whole field. See Pet. 8-9. The chilling effect of such a sweeping patent is obvious. The AMA warns that if patents like Prometheus's stand, physicians will be entangled in "a vast thicket of exclusive rights" to "basic diagnostic information" that is "critical" to "providing

sound medical care," to "the detriment of the nation's health." AMA Br. 5-6, 20-21; see Quest Br. 15-16 (research into "more precise reference range[s]" or "other metabolites" will be "strongly deterred").

This case therefore squarely presents the issue whether a mental step that preempts a physician's judgment involving biologic correlations becomes patentable under Section 101 because it comes at the end of a "process" that consists simply of administering existing drugs and testing blood for metabolites using existing tests. *E.g.*, Opp. 21-22 (conceding question is whether Prometheus's patent on "a truth" about "the physical world" is saved by preliminary "process steps that require concrete human actions").

There is no need for Mayo "to import novelty analysis into § 101" (Opp. 16) to establish that the first two steps of Prometheus's claims are trivial and cannot save the final mental step. As in *LabCorp*, Prometheus has "simply described the natural law at issue in the abstract patent language of a 'process,'" but "[t]he question is what those steps embody." And here as in *LabCorp* that "process is no more than an instruction to read some numbers in light of medical knowledge." 548 U.S. at 137; see *Funk Bros.*, 333 U.S. at 130-132 (where "qualities are the work of nature," "packaging" that makes no difference to the way the natural principle operates is "not enough").

2. The Federal Circuit attached dispositive significance to two "transformations"—changes in the human body resulting from administration of drugs, and changes in the blood when it is tested for metabolites. Pet. App. 17a-18a, 21a-23a. The court of appeals found these "transformations" "central to the claims," because "mental steps" of thinking about a dosage adjustment "alone are not patent-eligible."

Pet. App. 19a, 21a. But these changes are not transformative in any meaningful sense, or part of any invention by Prometheus. They are merely the ordinary elements of medical research and treatment. Any physician seeking to improve Prometheus's criteria would inevitably go through the same preliminary steps, so they neither limit the scope of the claims nor prevent them from preempting all uses of the natural correlations.

By once again making these well-known and ubiquitous preparatory steps into the touchstone of patent eligibility, the Federal Circuit ignored the teachings of *Bilski*. This Court held in *Bilski* that while the presence of a "transformation" is a "clue" to patent eligibility, it is not talismanic and does not override the principle that "laws of nature" must be free for all to use. 130 S.Ct. at 3225-3226; see *id.* at 3235 (Stevens, J., concurring), 3258 (Breyer, J., concurring). It stressed too that the antidote to "attempts to call any form of human activity a 'process'" is insistence that claims "mee[t] the requirements of § 101." *Id.* at 3226. And it refused to "endors[e] interpretations of § 101" that the "Federal Circuit has used in the past." *Id.* at 3231. None of those warnings stopped the Federal Circuit from adopting the same analysis as before this Court's GVR, again giving dispositive effect to commonplace transformations and turning a vast swath of ordinary medical practice and research into Prometheus's private fiefdom.

3. The Federal Circuit's decision rests on an indefensible reading of this Court's preemption decisions. It is well established that a patent that preempts all uses of a natural phenomenon does not satisfy Section 101. See *Benson*, 409 U.S. at 71-72 (claim is patent-ineligible when its "practical effect"

is "a patent on the [natural phenomenon] itself"); *Funk Bros.*, 333 U.S. at 130; *Chakrabarty*, 447 U.S. at 309; *LabCorp*, 548 U.S. at 135-136; *Bilski*, 130 S. Ct. at 3230, 3253, 3258. In analogizing Prometheus's claims to *Diehr*, the Federal Circuit made an error that nullifies the distinctions this Court has laid down to guide application of Section 101. Pet. App. 12a. Prometheus merely repeats that error.

The *Diehr* patent recited an algorithm that is a natural phenomenon, but narrowly confined the scope of the patent by reciting a particularized use of the equation to open and close a mold. The patent thus left others completely free to make different uses of the algorithm, with the result that there was no preemption of any natural law. Unlike the patentee in *Diehr*, Prometheus did *not* recite a particular use of the natural correlation. Its patents cover use of that correlation in every manner possible, including by developing criteria that are better than Prometheus's, thinking about why different criteria apply to different diseases, or exploring whether different metabolites can be measured and produce different criteria. They therefore fail the preemption standard set forth in *Benson* and *Flook*, in which claims were invalidated because they covered all uses of the computations.

4. Prometheus incorrectly asserts (at 30-31) that "*LabCorp* presented different issues" from this case. In legally relevant respects, the claims this Court agreed to review in *LabCorp* were identical. And even though Justice Breyer's opinion in *LabCorp* carefully analyzed this Court's relevant precedents and was cited approvingly by five members of the Court in *Bilski* for its substantive discussion of patent law (see Pet. 17-18), the Federal Circuit dismis-

sively "decline[d] to discuss a dissent" or address its analysis of preemption. Pet. App. 16a n.2.

Prometheus argues that the *LabCorp* patent did not involve administering a drug as the initial step of a "process." But the steps in *LabCorp* were testing a patient's body fluid to determine the level of an amino acid, then correlating that level with a deficiency in vitamins "such that any doctor necessarily infringes the patent merely by thinking about the relationship after looking at the test result." 548 U.S. at 132. The *LabCorp* claimant argued that, although any test might be used and the correlation was a natural phenomenon, the "process" combining these steps was "an inventive diagnostic test." Oral Arg. Tr., No. 04-607, at 42 (U.S. Mar. 21, 2006). Petitioner there, as here, asked this Court to decide whether patenting this "process" monopolized a basic scientific relationship—a naturally occurring correlation between a substance in the body and patient health.

The initial step Prometheus adds to some claims—a step absent in any event from claim 46—is administration of a drug that Prometheus did not invent. That a synthetic drug is administered and biologically converted does not distinguish this case from *LabCorp*, where tested-for amino acids appeared naturally. Prometheus *concedes* that the difference between synthetic and natural promoters of a biologic change is immaterial. Opp. 30 n.7.

Prometheus has nothing to do with the drug administered, the metabolites into which the body naturally converts the drug, or the blood test used to determine metabolite levels. Those are part of "the storehouse of knowledge." *Funk Bros.*, 333 U.S. at 130. Including these preliminary steps in a "process" is a patent drafter's trick that provides no meaning-

ful distinction between this case and *LabCorp*. See *Diehr*, 450 U.S. at 192 (refusing to "allow a competent draftsman to evade the recognized limitations on the type of subject matter eligible for patent protection"). As the *LabCorp* dissenters explained, any conduct can be described as a "process" with "a series of steps," but the key legal question is "what those steps embody." 548 U.S. at 137-138. Here, as in *LabCorp*, they embody "a simple natural correlation" and do nothing to reduce the degree to which the claims preempt the use of that correlation. *Id.* at 136-137.

Prometheus also contends (at 30) that the *LabCorp* patent was directed at "observing," while Prometheus's patents are directed at providing "'diagnostic information'" for use in treatment. But the claim in *LabCorp* sought to exert "control over doctors' efforts to use [a natural] correlation to *diagnose* vitamin deficiencies in a patient," and the claimant argued that this was a "useful, concrete, and tangible result." 548 U.S. at 134, 136 (emphasis added). Both here and in *LabCorp*, the controlling legal principle is the same: observing test results to check for natural biologic correlations that inform a physician's diagnosis may not be monopolized by a patent that amounts to "an instruction to read some numbers in light of medical knowledge." *Id.* at 137.

5. Prometheus pretends (at 19-20) that Mayo challenges its patents simply because they include a "mental step." But the mental step in *these* patents broadly precludes thinking about a natural biologic correlation between metabolite levels and patient health. Prometheus's citations are therefore irrelevant. The claim in *Arrhythmia* "d[id] not encompass subject matter transcending what [the claimant] invented." 958 F.2d at 1059. In stark contrast, Prome-

theus admits that its claims foreclose *any* use of the correlation, even when researchers reject Prometheus's numbers (Opp. 27), and even when physicians reject as inappropriate dosage changes suggested by Prometheus's metabolite ranges. Opp. 24. In *Abele*, which upheld a claim that applied an algorithm to CAT scans, the claim did not encompass any mental step, and the court found *un*patentable another claim that preempted all uses of the algorithm. 684 F.2d at 908. And *Griffin* was a patent "interference" dispute over which of two parties invented first, in which Section 101 issues were not asserted or addressed by the court. 285 F.3d 1029.

6. Although this Court granted certiorari to resolve the question six years ago in *LabCorp*—and three Justices urged the importance of deciding the merits "sooner rather than later" (548 U.S. at 134)—Prometheus asserts that resolving it now is "premature." But Prometheus concedes (at 33) that, as the only court with appellate jurisdiction over patent appeals, the Federal Circuit "forge[s] consistent nationwide patent law." See 28 U.S.C. § 1295. The Federal Circuit issued full opinions in this case before and after *Bilski*, reaching the same result and using the same reasoning in each. Its decision is binding on district courts throughout the country, and on the Federal Circuit itself. See *Hometown Fin.*, 409 F.3d at 1365. Because the decision below has immediate nationwide impact—including in cases pending before the Federal Circuit that will now be decided under an incorrect legal standard (see Opp. 32 n.9)—immediate review is warranted. There is nothing to percolate.

Additional considerations make review appropriate now. The issue presented has been fully explored

in the Federal Circuit's opinions, the district court ruling they reversed, the dissenting opinion in *LabCorp*, and numerous amicus briefs on every side of the issue filed in the Federal Circuit and this Court here and in *LabCorp*. The issue is dispositive of this protracted litigation, squarely presented, and free of procedural defects. This case presents the ideal vehicle to decide a question of immense practical importance to healthcare providers, patients, and payors.

7. Nothing in 35 U.S.C. § 287(c)'s narrow exemption from infringement liability for certain "medical or surgical procedures" carried out by a physician addresses the scope of Section 101. Opp. 34; see *Bilski*, 130 S.Ct. at 3228-3229 (statute contemplating "some business method patents" does "not suggest broad patentability" of such methods). And Prometheus never explains how denying a patent for a law of nature that has been dressed up as a "process" by adding a few data gathering steps known to the entire medical profession could interfere with developments in personalized medicine. Opp. 35-36. The AMA warns (at 14) that, to the contrary, such broad patents "would stifle rather than incentivize developments" in this important new field by preempting "scientific observations underlying proper diagnosis and treatment." See Quest Br. 18-20 ("Personalized medicine" uses "genetic markers to predict" disease and "an individual's response to a particular therapy"—just what patents like Prometheus's would foreclose).

Delaying review of the Federal Circuit's faulty approach will adversely affect medical research and patient care, "inhibit[ing]" the exercise of "medical judgment," diverting medical resources to "searching

patent files" to avoid potential treble damages liability, and "rais[ing] the cost of healthcare while inhibiting its effective delivery." *LabCorp*, 548 U.S. at 138. These "special public interest considerations" (*ibid.*) are not theoretical but have immediate practical consequences for the medical profession and the patients it serves, as the AMA and numerous other medical associations attest in their brief urging review (at 9-16). For seven years patients have been denied the benefit of Mayo's test—developed because Mayo believed it more effective than Prometheus's test.

As leading scholars have explained, allowing patents on "abstract ideas," like taking mental note of biologic correlations, leads to claims over ideas "unknown to the inventor" and means "future inventors face *reduced* incentives because they have to obtain a license" to improve upon—or even disprove—the patented correlation. BESSEN & MEURER, PATENT FAILURE, at 199-200. The chilling effect on medical innovation is all the greater because "[t]he notice function" of patents "does not always work" and "[c]learance costs" are high. *Id.* at 8, 10. Indeed, core First Amendment freedoms of physicians and patients are at stake. See Pet. 33-34; ACLU Am. Br. in *Bilski*, No. 2007-1130, at 5-7, 14 (Fed. Cir. Apr. 3, 2008) (a patent like that in *LabCorp* is one "on pure thought or pure speech"). This Court should review the Federal Circuit's erroneous decision to ensure that the Nation's efforts to promote quality healthcare at reasonable cost are not thwarted by sweeping monopolies of basic medicine.

CONCLUSION

The petition for a writ of certiorari should be granted.

Respectfully submitted.

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