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

REPLY BRIEF FOR PETITIONERS

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REPLY BRIEF FOR PETITIONERS

Prometheus's patents violate Section 101 because they wholly preempt an observed correlation between drug metabolites and patient health. Contrary to Prometheus's arguments, its patents are not narrow in scope. Unless physicians or researchers pay Prometheus they are precluded from making *any* use of the correlation between thiopurine metabolite levels and human health in connection with virtually all autoimmune diseases. This is so even though the patents describe no patient treatment, mandate no change in dosage, and do not prescribe any other steps to be taken by physicians. The patents therefore have the forbidden effect of preempting all uses of a physical phenomenon across a vast range of activity. Like the process patents held invalid in *Flook*, patents with such broad preemptive effect cannot be saved by adding the "conventional" activities of administering a "well known" drug and conducting a "long prevalent" blood test. 437 U.S. at 590, 594; *Bilski*, 130 S. Ct. at 3231.

Unlike the process of molding rubber in *Diehr*, Prometheus's process does not confine a natural law within specific steps, as Section 101 requires. Its patents foreclose physicians and researchers from even thinking about the natural correlation to produce *better* medical tests and *more accurate* metabolite ranges. Prometheus cannot foreclose medical advances that require application of improved medical judgment to the same natural phenomenon.

Section 101 is intended to weed out such invalid patents at an early stage. If it fails to do so, the federal courts and Patent Office will be flooded with

similar overreaching claims, with no means to filter out those that impermissibly prevent doctors and researchers from thinking about a patient's natural reaction to a drug or other therapy. Physicians will face a thicket of overlapping patents that cover every facet of medical practice. The threat of costly and time-consuming treble damages litigation that cannot be resolved without a trial will deter medical research and hurt patients—just as Prometheus's suit has stifled physician access to Mayo's improved test and to Dr. el-Azhary's research showing that Prometheus's metabolite ranges are harmful for dermatology patients.

Unless Section 101 bars the drafter's trick of embedding a natural phenomenon in token steps that do nothing to narrow the range of preemption, all the ill effects that Justice Breyer identified in *LabCorp* are certain to occur, as the American Medical Association and other medical groups and laboratories have explained. Medical costs will increase as physicians divert resources to patent searches, licensing, and litigation; and medical care will suffer as doctors are deterred from exercising medical judgment that might infringe broad and open-ended patents like Prometheus's. Nothing in the briefs of Prometheus or others who would gut Section 101, turning legally defective patent claims into occasions for a jury trial or forced license, explains why Congress would have intended this extraordinarily damaging result.

A. The Patent Office's Contention That Prometheus's Admittedly Invalid Patents Satisfy Section 101 Clashes With This Court's Precedents.

The government agrees (at 27-29) that Prometheus's "patents themselves make clear" that "the 'administering' and 'determining' steps of the disputed claims were part of the prior art" and that "the inventors' only asserted innovation" is a final mental step that "add[s] no patentable weight" to the claims. Accordingly, the government acknowledges (at 11) that Mayo's contention "that the claims are invalid appears to be correct."

The government's assertion that Prometheus's patents should be invalidated under the Section 102 and 103 "novelty" and "non-obviousness" standards rather than under Section 101's patent-eligibility standard is inconsistent with this Court's precedents. It would guarantee that patents on natural phenomena—rather than being invalidated at the Section 101 threshold with the least chill on innovation—instead spawn complex factual inquiries that often could not be resolved short of trial. And it so undermines the effective provision of health care that it cannot conceivably be what Congress intended.

1. The Patent Office recognizes that a patent on a natural "correlation itself" would be ineligible under Section 101. Br. 23. But it contends that adding conventional data-gathering steps like blood testing that have been used routinely throughout the medical profession is enough to create a patent-eligible "process." Br. 13-17. That toothless standard would make Section 101 meaningless as a constraint on monopolization of natural phenomena, for as

Justice Breyer observed in *LabCorp*, any natural phenomenon can be dressed up with "a series of steps." The important question is "what those steps embody." 548 U.S. at 137-138. Here, as in *LabCorp*, the steps are just "an instruction to read some numbers in light of medical knowledge." *Ibid.* Prometheus's own amici concede that its patents cannot survive under the standard stated by Justice Breyer, and not rejected by any Justice, in *LabCorp*. See Myriad Br. 22, 26; Novartis Br. 5, 7, 29.

Because Prometheus's claims are nothing but "prior art" plus a step of thinking about numbers that "add[s] no patentable weight" (U.S. Br. 28-29), they embody nothing innovative or deserving of monopoly protection. See *Mackay Radio*, 306 U.S. at 94 (the "mathematical expression" of "a scientific truth" is "not a patentable invention"); *Flook*, 437 U.S. at 595 n.18 ("an improved method of calculation, even when tied to a specific end use, is unpatentable subject matter"); *Bilski*, 130 S. Ct. at 3221. Prometheus's patents are precisely the sort of facially invalid claims that should be rejected at the threshold.

2. This Court recently explained that "[i]f a high enough bar is not set" for process patents—which "raise special problems in terms of vagueness and suspect validity"—"patent examiners and courts could be flooded with claims that would put a chill on creative endeavor and dynamic change." *Bilski*, 130 S. Ct. at 3229; see *Graham*, 383 U.S. at 9 (Thomas Jefferson, author of the 1793 Act, "insisted on a high level of patentability"). The Patent Office's proposal to dilute the Section 101 inquiry, and make patentability turn on application of Sections 102 and 103, would have precisely that harmful effect.

A "unique element" of the Section 101 inquiry is that it can often, as here, "be addressed by examining the four corners of a patent application"—a stark contrast to "evaluating novelty and nonobvious subject matter," which usually involves "searching a very large and often uncertain record of prior art" that invites mistakes. BOHANNAN & HOVENKAMP, CREATION WITHOUT RESTRAINT, ch. 5, at 14; see Am. Br. of Nine Law Professors at 34-36. The government concedes (at 11) that whether Sections 102 and 103 are satisfied depends on "fact-intensive" litigation.

Section 103 requires "factual inquiries" into all "the circumstances"—including the "scope and content in the prior art"; the "level of ordinary skill in the pertinent art"; "commercial success"; "long felt but unsolved needs"; and "failure of others"—inquiries fraught with administrative "difficulties" and a lack of "uniformity." *Graham*, 383 U.S. at 17-18. Similarly burdensome inquiries are necessary to determine novelty under Section 102. *E.g.*, *Schumer* v. *Lab. Computer Sys.*, 308 F.3d 1304, 1315-1316 (Fed. Cir. 2002). Not surprisingly, despite the government's view that the patents here show facial legal defects, Prometheus promises to "litigate all of these issues fully," arguing that their "complexity" makes them "'the most elusive'" questions in "'all of patent law.'" Prom. Br. 46-48. For the government to invite lengthy litigation over patents it concedes are invalid is contrary to sound antitrust policy. See *Walker Process Equipment, Inc.* v. *Food Mach. & Chem. Corp.*, 382 U.S. 172, 177 (1965).

The government's argument is doubly impractical because there is nothing comparable under Sections 102 and 103 to the well-developed body of

case law from this Court addressing the "natural phenomenon" issue at the heart of this litigation or expounding on what must remain in the "public domain" under Section 101. See *Bilski*, 130 S. Ct. at 3227; *id.* at 3258 (Breyer & Scalia, JJ., concurring). The poor fit of these provisions also is shown by the fact that the Patent Office granted the patents it now concedes "likely warrant invalidation" without perceiving any obstacle under Section 102 or 103. U.S. Br. 26.

The government's proposal to reduce Section 101 to a rubber stamp that is easily satisfied with clever drafting, and to have the federal courts grapple instead with complex inquiries that are difficult to resolve, is flatly at odds with Congress's goals in this year's America Invents Act, Pub. L. 112-29, 125 Stat. 284 (Sept. 16, 2011). Congress there responded to "a growing sense that questionable patents are too easily obtained" and "too difficult to challenge," and sought to "mov[e] in the direction of improving patent quality and making the determination of patent validity more efficient." H.R. REP. NO. 112-98, at 39 (June 1, 2011). In requiring "a more efficient system for challenging patents that should not have issued," it aimed to "limit unnecessary and counter-productive litigation costs." *Id.* at 39-40. A new procedure for post-grant review by the PTO that includes patent-eligibility under Section 101 is designed to minimize litigation burdens, and new fees provide the PTO with resources needed to weed out over-broad claims. *Id.* at 45, 48-50.

It is contrary to these goals to allow the PTO and the Federal Circuit to reduce the rigor of the Section 101 inquiry in a case of this kind. The government offers not a word in defense of Prometheus's patents.

It admits (at 8, 11, 27-29) that "the patents themselves make clear" there are "powerful arguments against affording patent protection to respondent's process." Yet after seven years of costly litigation, and two trips to this Court and the Federal Circuit, it argues that more judicial proceedings are necessary under Sections 102 and 103. In the future, as has happened in this case, the public would be exposed to monopoly overcharges and forgone medical services while decade-long litigation lumbers forward, contrary to the teaching of *Bell Atlantic* v. *Twombly*, 550 U.S. 544 (2007), *Celotex* v. *Catrett*, 477 U.S. 317 (1986), and the America Invents Act, all of which favor swift and efficient invalidation of defective patent monopolies. See *Brenner*, 383 U.S. at 532 (interpreting Patent Act to require invalidation in light of the "general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other").

The district court faithfully applied the Patent Act principles laid down by this Court when it granted summary judgment. Whether or not the Patent Office intends to apply Section 101 rigorously in its own proceedings, as Congress intends, it should not oppose efficient summary judgment proceedings in federal district court.

B. Prometheus's Patents Broadly Preempt Use Of A Natural Phenomenon.

Prometheus pretends its patents are "narrow and specific," apply only to "actual medical treatment," and do not preempt "fundamental concepts" or "any substantial activity." Br. 25, 32-33, 41-46. But it successfully advocated a far broader construction of its patents in the courts below. And the limitations Prometheus points to are illusory. As the

government observes (at 23), Prometheus's patents "preempt substantially all" of the "practical applications" of the correlations they describe.

1. Although the database used to develop these patents related only to pediatric gastrointestinal disorders, Prometheus concedes that its claims cover *all* autoimmune conditions. Br. 6-9. These include, in addition to gastrointestinal disorders, rheumatoid arthritis, lupus, hepatitis, diabetes, pernicious anemia, skin diseases, and a host of other conditions listed in the patents to "illustrate, but not limit" the scope of the claims. 2JA 13-14, 31-32; Pet. App. 51a, 75a; *e.g.*, 2JA 17, claim 22 (claiming method covering *any* non-gastrointestinal autoimmune disease).

Prometheus says the patents are narrow because some diseases are not covered. Br. 42-43; see U.S. Br. 22. But thiopurine drugs are immuno-suppressive, so the patent covers *all* autoimmune conditions that could be treated with the drugs except the narrow areas of organ transplantation and leukemia. See 1JA 27, 34. Prometheus cannot make natural correlations patentable by limiting its claims to one broad class of diseases. As *Bilski* explains, "*Flook* established that limiting an abstract idea to one field of use" does "not make the concept patentable." 130 S. Ct. at 3231; see *Diehr*, 450 U.S. at 193 n.14 ("A mathematical formula does not suddenly become patentable subject matter" by "limiting the reach of the patent" to "a particular technological use").

Confirming the broad sweep of its claims, Prometheus argues (at 43) that within the class of autoimmune diseases, physicians would have to invent radically new methods of calibrating metabolites to escape preemption. Using a standard blood test and

reaching their own conclusions—as physicians have done for decades—would not be lawful.

Given this broad preemption of all practical uses of the correlation between metabolites and health, Prometheus's amici attack a straw man when they argue that Mayo is challenging medical patents generally. We nowhere contend that Section 101 "excludes medical processes" (PhRMA Br. 8), "diagnostic and therapeutic methods" (BIO Br. 2), or patents involving correlations (AIPLA Br. 17). Mayo readily acknowledges the value of patent protection for innovations that "entail extraordinary risk and expense on the part of the pharmaceutical and biotechnology industries." PhRMA Br. 3-4. But the challenged patents here are invalid because they are uniquely abstract and expansive in their attempt to preempt a physical phenomenon. The rule that Justice Breyer embraced in *LabCorp* and that Mayo advocates here does not call into question patents that lack these pernicious features.

2. Prometheus also contends (at 43) that competitors are free to use numbers departing from its range by more than 15%. The government says doctors remain free to use higher correlations because "Crohn's disease patients may comfortably tolerate much higher 6-TG metabolite concentrations than those disclosed in the patent." U.S. Br. 22. But Prometheus successfully argued in the district court that its claims to levels "greater than" the number specified in the patents means the levels have no upper bound but reach "infinity." Sept. 29, 2005 Hearing Tr. at 49, D. Ct. Dkt. 605; see Pet. App. 96a-97a (holding that because "no upper limit is mentioned in the patents," "such limitation cannot be considered in construing the terms of the patent

claims," which cover "any level that is above about 400"); 2JA 17, claims 32-36 (there is no upper limit when thioguanine is administered).

Even under Prometheus's reasoning, its patents would prevent a physician from concluding that a 7000 6-MMP reading indicates too toxic a dose of these life-threatening drugs and that a 14% reduction in the maximum limit, to 6000, is necessary for patient safety. The tasks doctors and researchers have always performed in this fast-moving field—test blood and think freely about what the results mean—can now only be performed by paying Prometheus a fee.

3. Contrary to Prometheus's assertion (at 32) that the patents operate "in the context of patient treatment," claim 46 monopolizes the two-step process of determining metabolite levels and thinking about what that means for dosage. Prom. Br. 9 n.7. And Prometheus successfully argued to the district court—whose construction of the claims was adopted by the Federal Circuit—that the final step does not require *any* dosage change if a physician is notified that a dosage adjustment *may* be required. Pet. App. 109a; 1JA 13. Accordingly, only testing for metabolites and thinking about an appropriate dosage is required for infringement—exactly what a non-treating physician would do when conducting research.

Prometheus's attack on Dr. el-Azhary confirms that its claims are not limited to treatment. Prometheus concedes (at 11) that it alleged infringement based specifically on Dr. el-Azhary's research. Dr. el-Azhary's purpose in collecting data on metabolite levels was to study optimal levels for dermatology patients with autoimmune conditions. 1JA 17-18.

Metabolite levels for gastrointestinal disease were "irrelevant" to her. 1JA 19. But because Prometheus's claims applied to *all* autoimmune diseases and Dr. el-Azhary had *once* been sent a document identifying Prometheus's range (1JA 21, 38-39), Prometheus argued that she infringed when she thought about the best range for dermatology patients—"[w]hether she crumples [up the document], throws it away, reads it, acts on it, doesn't act on it, any assumptions you want." 1JA 42.

Dr. el-Azhary was deposed at length; forced to turn over confidential patient records; accused of infringing when she researched different ranges for dermatology patients; and dared not publish her results—which showed that the proper range for dermatology diseases was *vastly* different from Prometheus's ranges (Mayo Br. 13)—because Prometheus sought an injunction that would have covered that alleged infringement.

Prometheus runs away from these allegations now (at 11 n.12). For the first time in this litigation it says that Dr. el-Azhary did not infringe if she "ignored" or "disbelieved" Prometheus's numbers. That new standard, which is nowhere stated in the patents or found in the record, would inject a vague mental element into the issue of infringement and could not give any practical assurance to a physician. As Dr. el-Azhary testified at her deposition, once she knew of Prometheus's numbers, she could not "rule out" that she had them in mind when investigating whether other ranges were better for dermatological diseases. Sept. 21, 2006 Depo. at 96. Beyond this, the record is clear that Prometheus contended below—without any exceptions for "ignoring" or "disbelieving"—that once Dr. el-Azhary learned of

Prometheus's correlations she could not escape infringing when she thought about whether those numbers were right for dermatology patients and concluded they were not. Pet. App. 77a n.10; 1JA 5-6, 17-22, 36-42.

Even accepting at face value Prometheus's about-face regarding the construction of its claims, the fact remains that it seeks in this litigation to prevent Mayo from offering a more cost-effective test with different numbers, different services, and different guidance. And even if some use of the correlation were possible outside these two patents, on its theory Prometheus or others could replicate these patents for different fields so that any remaining area would be monopolized too. Indeed, Prometheus has secured from the Patent Office six *more* patents on this correlation since filing suit in 2004.[1]

That thicket of patents on a single correlation confirms what the AMA has pointed out: if Prometheus's patents are valid, there will be a flurry of patent applications seeking to monopolize *every* facet of medical research and practice. A patentee could claim monopoly profits and stave off new research and services while it mounted decade-long treble damages litigation. See James Bessen *et al.*, *The Private and Social Costs of Patent Trolls*, Boston U. School of Law Working Paper (Sept. 19, 2011) (citing $80 billion a year of lost wealth to patent defendants, substantially reducing their incentive to innovate). Few researchers and hospitals could afford to run the enormous risks and costs of such litigation.

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[1] See U.S. Patents Nos. 8,030,293, 7,625,876, 7,429,570, 7,425,546, 7,326,694, and 7,105,497 (dating from 2005-2009).

C. The Patents Are Not Saved By The Miscellany Of Defenses Offered By Prometheus.

1. Prometheus contends (at 41-42) that the correlation between metabolite levels and human health is not "natural" because it is a response to administration of synthetic drugs, which are the product of human ingenuity. But thiopurine drugs are not the result of *Prometheus's* ingenuity; they have been used for several decades. And Prometheus's claims do not cover the synthetic drugs, but rather the body's natural response to those drugs. The process by which the body metabolizes the drugs is indisputably a natural phenomenon, as acknowledged by Prometheus's expert and both courts below. Pet. App. 15a, 65a. This Court's decisions make clear that "'physical phenomena'" cannot be patented, and the body's response to a chemical unquestionably falls into that category. *Bilski*, 130 S. Ct. at 3225. Even if expert chefs exercise ingenuity in preparing high-fat meals, the body's generation of cholesterol is a natural phenomenon that all doctors are free to examine and correlate. Prometheus previously conceded that nothing turns on whether the drug is synthetic or natural. Br. in Opp. 30 n.7.

This Court never has held that someone else's ingenuity, or the mere existence of human intervention, warrants a patent monopoly on a physical phenomenon. The claims in *Funk Brothers* were unpatentable even though the mutually inhibitory mix of bacterial strains existed only because of human ingenuity. And the process claim held invalid in *Flook* covered a catalytic conversion that was entirely the product of human ingenuity, and included as a critical "step" the act of measuring

temperature. Here, as in *LabCorp*, the patents improperly monopolize a natural metabolic process. Prometheus's claims covering the physical phenomenon are not patentable simply because human intervention was necessary to develop and administer the drug.

2. Like the Federal Circuit, Prometheus (at 25-27) and the government (at 13-15) assert that thiopurine drugs "transform" a patient's body chemistry, testing for metabolites "transforms" the patient's blood, and the "transformative nature of the process as a whole" satisfies Section 101 even though the administering and determining steps—to which Prometheus made no contribution—are conventional steps that are necessary to observing the phenomenon. According to Prometheus (at 25), a process including these commonplace transformations "*necessarily* constitutes a concrete application" of scientific knowledge that satisfies Section 101—a return to "transformation" as the touchstone of patentability. But *Bilski* made clear that transformation is only a "clue" to patentability: not every transformation satisfies Section 101. 130 S. Ct. at 3225.

This is shown by *Flook*, where chemical transformations that occurred during the catalytic conversion of hydrocarbons did not save the broad claim invalidated there. Here too, the "transformations" the court identified are an exercise in labeling that bear no relationship to the purposes of the patent laws—the body itself produces the metabolites and blood testing is conventional. And these transformations do nothing to narrow the preemptive effect of the patents. As Justice Breyer has explained, using "virtually any natural phenom-

enon for virtually any useful purpose" involves "transforming matter." *LabCorp*, 548 U.S. at 136.

Prometheus says the transformations are "integral to the patents' core purpose" (Br. 26), but administering drugs and testing blood are commonplace data-gathering steps. And this Court has made clear that conventional data-gathering steps do not create a patentable process out of a natural phenomenon. See *Bilski*, 130 S. Ct at 3231 ("token" extra-solution components that provided "inputs into [an] equation" did "not make [a] concept patentable"); *Flook*, 437 U.S. at 590. Accordingly, this Court rejected a process patent that combined "the abstract idea of hedging risk in the energy market" with instructions to use "well-known random analysis techniques" to provide data inputs. *Bilski*, 130 S. Ct. at 3231. Similarly, Prometheus's addition of conventional administering and determining steps does not allow it to monopolize natural correlations just because those steps involve transformations of matter.

In fact, the two steps Prometheus added would be needed to make *any* use of the correlations. Without administering the drug and testing blood there would be no data to correlate. Thus, these steps are no limitation at all. See *In re Richman*, 563 F.2d 1026, 1030 (C.C.P.A. 1977) (steps that "merely determine values for the variables used" in making calculations "do not suffice to render the claimed methods, considered as a whole, statutory subject matter"); *In re Grams*, 888 F.2d 835, 840 (Fed. Cir. 1989) (rejecting under Section 101 claims that involved "performing clinical tests on individuals to obtain data"). The happenstance that these data-collection steps involve transformations should not

make them predicates for patentability because they are not inventive and do not narrow the preemptive sweep of the claimed monopoly.

Prometheus also points (at 27) to the use of "machines" to test blood, but it contributed nothing to the invention of those machines or to any new way to use them—exactly the situation in *Benson* and *Flook*. And their use is merely incidental to the claim covering natural correlations. Prometheus even argues (at 42) that because thiopurine drugs could be patented by their inventor as a "composition of matter," any process tied to those drugs must be patentable. But if "a tie to" any machine, transformation or composition of matter developed by others were enough to patent a physical phenomenon, any law of nature could be monopolized, contrary to this Court's decisions.

3. Prometheus's reliance (at 21, 27-28, 30) on Section 101(b), which defines "process" to include "a new use" of a machine or composition of matter, is completely misplaced because this definition does not alter the physical phenomenon rule laid down in *Flook* and *Bilski*. And thiopurine drugs and testing blood for metabolites are not "new uses." Prometheus concedes that physicians long have known that thiopurine metabolite levels provide "valuable information" about dosage; that technology to measure metabolites has long existed; and that its claims merely posit a contestable range of numbers for those metabolites. Prom. Br. 4, 11 n.13; 2JA 1-3, 10 col. 8:37-46, 19-21. Studies published years before these patents confirm that physicians across "North America" used and "value[d] these measurements." Summary & Reply, Cuffari *et al.*, *6-MP Metabolite Levels: A Potential Guide to Crohn's Disease Therapy*,

113 GASTROENTEROLOGY 690, 692 (1997); see Mayo Br. 5. Attaching particular numbers to a physical phenomenon and telling physicians to think about those numbers adds no "new use," but merely monopolizes what physicians already routinely do.

Contrary to Prometheus's and the government's arguments, Mayo does not contend that the "administering" and "determining" steps should be "ignored." But when the "claim as a whole" consists of nothing but these conventional steps plus a mental step of thinking about resulting numbers that the government concedes "add[s] no patentable weight" to the claims (U.S. Br. 28-29), it is clear that the claim *as a whole* is not patentable. See *LabCorp*, 548 U.S. at 137-138.

Under the government's and Prometheus's approach even laws of nature like $E=mc^2$ would be patentable. Simply combining that formula with a well-known computer program (a machine) or well-known process for isolating a sample of matter (a transformation) would satisfy Section 101. Because the law at first discovery was unknown and not obvious, Sections 102 and 103 would not stand in the way of a patent. But Einstein could *not* patent his original and valuable formula $E=mc^2$. *Chakrabarty*, 447 U.S. at 309. And it is absurd to suggest that Prometheus can patent "400=something to think about." Adding an ordinary blood test does nothing to elevate this open-ended mental step.

4. Prometheus's claims were not approved by Congress when it enacted 25 U.S.C. § 287(c). That provision cuts off remedies for infringement brought against "medical practitioners" and "affiliated entities" for the performance of a "medical" procedure. See Prom. Br. 57-58. Section 287(c) says nothing to

validate patent monopolies over observing how the human body responds to an external stimulus. It cannot be read to imply that Congress thought such patents proper. See *Bilski*, 130 S. Ct. at 3228-3229 (statutory defense specific to business method patents implies that there may be such patents but does "not suggest [their] broad patentability").

Vague references to "settled expectations" arising from the PTO having granted 150,000 patents for "methods of treating patients," or to particular medical patents, are also unavailing—the more so because the government admits that the PTO overlooked fatal defects in the patents it granted here. U.S. Br. 16; Prom. Br. 50-51. There is no reason to think that many granted patents claim broad preemption of a physical phenomenon, as Prometheus's do. And if some do so, the public is entitled to protection from them.[2]

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[2] For example, the patents at issue in *Arrhythmia* and *Abele* (Prom. Br. 47, 52) did not include a mental step that broadly precluded physicians from thinking about natural correlations. The claim in *Arrhythmia* "d[id] not encompass subject matter transcending what [the claimant] invented." 958 F.2d at 1059. The claim upheld in *Abele* did not include any mental step, and the court held *un*patentable another claim that preempted all uses of an algorithm. 684 F.2d at 908. *LabCorp* is the only case cited by Prometheus and its amici involving a similar patent.

Two recent Mayo patents cited by Prometheus (at 57) are different from its own overbroad claims. They focus on novel processes without preempting any natural phenomena. See U.S. Patent 7,981,612 (method involves performing traditional follow-up testing after making an initial determination with novel DNA testing); U.S. Patent 7,998,670 (process uses a novel man-made DNA probe that does not preempt any activity previously in the public domain). The third patent cited by

D. This Court's Decisions Require Invalidation Under Section 101.

The mental step in Prometheus's claims broadly precludes physicians from thinking about correlations produced naturally by the body in response to drugs—effectively barring new and improved testing in this rapidly changing field of medicine for twenty years. The government agrees with Mayo that this mental step "add[s] no patentable weight" to the claims, which otherwise consist of conventional steps employed in a conventional way.

Prometheus nonetheless relies on *Diehr* as supporting the patentability of its claims. But the contrast between the claims here and in *Diehr* could not be starker. The *Diehr* patent confined an equation within a particular manufacturing process which ensured that rubber molds were opened at the right moment to perfect the cure—a narrow but important solution to an industrial problem to which there is no equivalent in Prometheus's claims. Doctors knew how to administer drugs, test blood, and consider metabolite levels long before hearing from Prometheus. And rather than an open-ended claim on thinking about a biological correlation, the *Diehr* patent left others completely free to make different uses of the equation, with the result that there was no preemption of natural law.

This Court has never drawn a distinction between foreclosing use of "truly fundamental principles, in the abstract and across a broad range of potential endeavors and future applications," and

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Prometheus (at 51-52) expired in 2003. See http://tinyurl.com/3bn6u6g.

foreclosing most practical uses of a "natural phenomenon." Prom. Br. 37-39. To the contrary, it has repeatedly stated that "phenomena of nature" cannot be monopolized with broad claims because "they are the basic tools" of science. *Benson*, 409 U.S. at 67. Prometheus's effort to distinguish between "truly fundamental" and other laws of nature is unsupported in the case law, in which the scope of preemption of physical phenomena is key.

Here, as in *O'Reilly*—which prohibited Samuel Morse from expanding his patent on the telegraph to all uses of electric current for transmitting characters—Prometheus impermissibly claims "an exclusive right" to control anything a physician might do with metabolite correlations over a broad field, based on a narrow and highly disputable discovery. It impermissibly seeks to turn observation of metabolite levels in a database of pediatric Crohn's disease patients into a wide-ranging bar on physicians using their judgment in relation to dozens of diseases suffered by millions of people. See *Minerals Separation*, 242 U.S. at 271 (invalidating patent claims and holding that process patents "must be confined" to the "proportions" actually discovered). As in *Benson*, the "practical effect" of Prometheus's patents is that anyone who wishes to make use of the natural correlation between metabolite levels and the health of any patient with an autoimmune condition must pay Prometheus a license fee. It is effectively a patent on "the [natural correlation] itself," deterring further research—in what had been a fast-developing area—that could save lives. 409 U.S. at 71-72.

Prometheus treats *Flook* as a dead letter (at 29), "unequivocally rejected" in *Diehr*. But this Court

cited *Flook* repeatedly in *Bilski* as a guide to determining whether claims "are not patentable processes because they are attempts to patent abstract ideas." 130 S. Ct. at 3229-3230. The Court specifically endorsed the holding of *Flook* that when "an application's only innovation was reliance on a mathematical algorithm," embedding that algorithm in "'a particular technological environment'" and adding conventional extra-solution steps did not satisfy Section 101. And it applied that rule to strike down the inventor's business method claims. *Id.* at 3230-3231. As in *Bilski*, the claims here "add even less to the underlying [law of nature] than the invention in *Flook* did, for the *Flook* invention was at least directed to the narrower domain of signaling dangers in operating a catalytic converter." *Id.* at 3231. Prometheus's patents preempt even thinking about a biological correlation across the entire range of its practical application, for all patients taking immuno-suppressive drugs for virtually all auto-immune conditions.

Prometheus relies (at 39) on other cases that are irrelevant here because the patents, as in *Diehr*, narrowly confined a scientific principle within a process that left other uses freely available. The patentee in *Tilghman* "was the original discoverer of [a] process" for manufacturing fats and oils using specific applications of hot water under high pressure. 102 U.S. at 713. *Neilsen* upheld a patent on a mechanical apparatus for blowing hot air into a furnace, having discovered that hot air worked better than cold. See *id.* at 724-725; 151 Eng. Rep. 1266 (Exch. 1841). Bell's discovery of an apparatus that modulated electric current to reflect sound waves over a closed circuit left room for infinite other uses of electricity. *Telephone Cases*, 126 U.S. at 532-535.

Prometheus, by contrast, preempts all practical uses of the principle that thiopurine drugs, naturally converted by the body to metabolites, correlate with patient health and it insists that its patented numbers bar other researchers from offering cheaper tests with more accurate and useful information. *Flook* and *Bilski* hold that such sweeping preemption is inconsistent with Section 101.

E. Invalidating Prometheus's Patents Would Encourage, Not Hinder, Personalized Medicine.

New methods of testing or treating patients often are patent eligible. But combining existing drugs and blood testing with broad claims covering the relationship between drug metabolites and health does not pass muster. Sustaining Prometheus's patents would open the door to obviously abusive claims encompassing, for example, administering a drug, taking body temperature, and considering a change of dosage if body temperature exceeds 98.6 degrees. See AMA Am. Br. 12. Invalidating them under Section 101 would in no way call into question patents for innovative methods of treating patients, such as "new pharmaceuticals, medical devices" or "diagnostic testing kits," which are far removed from the instruction to think about physical phenomena at issue here. *Id.* at 10-11. Furthermore, this Court has not hesitated to reverse erroneous Federal Circuit interpretations of the Patent Act despite patentees' predictions that doing so would upset "millions of patents" and "tens of billions of dollars" in investment. *E.g.*, *KSR Int'l Co.* v. *Teleflex Inc.*, 550 U.S. 398 (2007); Br. of Respondent, No. 04-1350, at 15.

It is those inventions of new drugs, machines, or test equipment that require the incentives of a

patent monopoly, as amici and the literature Prometheus cites confirm. *E.g.*, Roche Am. Br. 7-11; FTC, EMERGING HEALTH CARE ISSUES 4 (2009); see PRESIDENT'S COUNCIL, PRIORITIES IN PERSONALIZED MEDICINE 21 (2008) (patent protection is necessary to encourage "large, high-risk R&D investments" in "novel medical products"; by contrast, an attempt to "patent diagnostic correlations" is "doubt[ful]" based on "Supreme Court cases"); Mayo Br. 49-50.

Prometheus says (at 53) that doctors using its methods can calibrate thiopurine dosages faster and cheaper than before. But Mayo investigated metabolite levels and proved Prometheus's numbers were wrong—Prometheus later abandoned its upper limit of 7000 for 6-MMP and adopted Mayo's 5700 limit. Dr. el-Azhary found that Prometheus's numbers were far in excess of safe levels for dermatology patients. Mayo sought to market a considerably less costly test based on its improved numbers, in obedience to the ethical mandate that physicians shall "do no harm." Prometheus would cut off those benefits to patients for twenty years based not on a large investment—it made none (Mayo Br. 4-6)—or on a significant discovery, but based merely on administering known drugs, testing blood using known methods, and observing a physical phenomenon that is part of the storehouse of knowledge open to all researchers. See SECRETARY OF HEALTH & HUMAN SERVICES' ADVISORY COMMITTEE REPORT 2 (finding *no* case in which a patent was necessary for development of a genetic test).

The district court properly applied this Court's precedents under Section 101 when it protected the public against this overreaching claim.

CONCLUSION

The judgment of the court of appeals should be reversed.

Respectfully submitted.

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