No. 09-

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.

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

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

The Federal Circuit, reversing the district court, upheld Prometheus's patent claims covering a process for correlating the level of certain chemicals in a patient's blood with the patient's health. By those claims, Prometheus seeks to monopolize the use of blood tests in the research, diagnosis, and treatment of disease, such that a physician violates the patent merely by thinking about the correlation between the test results and the patient's health or treatment. This Court granted certiorari to determine whether basic scientific relationships may be monopolized in this way in *Laboratory Corp. of Am. Holdings* v. *Metabolite Labs., Inc.*, 548 U.S. 124, 135 (2006) ("*LabCorp*"), but dismissed the writ for lack of adequate issue preservation. Dissenting from dismissal, Justices Breyer, Stevens, and Souter explained that such patents are invalid under this Court's precedents, and that resolving the issue presented in *LabCorp* was of great importance to innovative scientific inquiry and effective medical research and treatment.

The question presented is as follows:

Whether 35 U.S.C. § 101 is satisfied by a patent claim that covers observed correlations between patient test results and patient health, so that the claim effectively preempts all uses of these naturally occurring correlations.

RULES 14.1(b) AND 29.6 STATEMENT

All parties are identified in the caption of this petition. Petitioner Mayo Collaborative Services, a subsidiary of Mayo Clinic, is a for-profit Minnesota corporation that provides reference laboratory services under the name Mayo Medical Laboratories. Petitioner Mayo Clinic Rochester, a subsidiary of Mayo Clinic, is a charitable, nonprofit corporation located in Rochester, Minnesota. No publicly held company owns 10% or more of the stock of either petitioner.

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PETITION FOR A WRIT OF CERTIORARI

Petitioners, Mayo Collaborative Services (d/b/a Mayo Medical Laboratories) and Mayo Clinic Rochester (collectively, "Mayo"), respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The court of appeals' opinion (App., *infra*, 1a-25a) is reported at ___ F.3d ___, 2009 WL 2950232 (Fed. Cir. 2009). The district court's opinion (App., *infra*, 26a-59a) is reported at 2008 WL 878910 (S.D. Cal. Mar. 28, 2008).

JURISDICTION

The court of appeals entered its judgment on September 16, 2009. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101.

"The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." 35 U.S.C. § 100(b).

INTRODUCTION

This Court previously granted certiorari on the issue presented in this case in *Laboratory Corp. of America Holdings* v. *Metabolite Laboratories, Inc.*, 548 U.S. 124, 135 (2006) ("*LabCorp*"), but could not resolve the merits because petitioner there had not preserved the issue. The patent claims in *LabCorp* and Prometheus's claims here both attempt to exclude the public from using the results of basic human metabolic testing in the research, diagnosis, and treatment of disease. They do so by claiming protection for the process of recognizing a correlation between the level of certain chemicals in the patient's blood and the patient's health. In both cases, the claims are silent as to what should be done with such correlations and as a result purport to cover and thus preempt all possible uses of the biological correlations.

Applying this Court's case law invalidating patent claims that preempt all uses of a fundamental scientific principle, the three Justices who dissented from the dismissal of *LabCorp* as improvidently granted reasoned that the claims at issue were obviously invalid and not even "at the boundary" of patentability. The district court here reached the same conclusion with respect to Prometheus's claims. The Federal Circuit reversed without even considering the reasoning in *LabCorp*, using a newly minted "machine or transformation" test in place of this Court's established standards for patentability.

This Court should review the Federal Circuit's erroneous decision, which is inconsistent with this Court's precedent and with the reasoning of three Justices in *LabCorp*. As reflected in the grant of certiorari in *LabCorp*, the 20 amicus filings in that

case, and the seven amicus filings in the Federal Circuit here, the issue is one of exceptional public importance. Justices Breyer, Stevens, and Souter explained that "special public interest considerations" are implicated by the question presented because overbroad patents will "inhibit doctors from using their best medical judgment," "force doctors to spend unnecessary time and energy to enter into license agreements," "divert resources" from healthcare tasks to "the legal task of searching patent files," and "raise the cost of health care while inhibiting its effective delivery." 548 U.S. at 138. These considerations again warrant this Court's review, which may now proceed without the problems that prevented resolution in *LabCorp*.

STATEMENT

A. Prometheus's Sweeping Patent Claims

Prometheus's broad patent claims attempt to turn a physician's thought processes into infringement. Specifically, the claims encompass a physician's mental determinations when evaluating a patient who has been given a thiopurine drug.[1] Enzymes in the human body metabolize such drugs naturally into metabolites that are therapeutically active. App., *infra*, 41a. Low levels of such metabolites indicate an insufficient dose of the drug, whereas high levels indicate too much. These facts have been understood by physicians for decades, as the Prometheus patents concede. See, *e.g.*, '623

[1] U.S. Patents 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent"), reproduced at C.A. App. A10001 and A10019, are also available at http://tiny.cc/y867p and http://tiny.cc/TR2FY, respectively.

Patent at 8:37-39, C.A. App. A10010 (citing "[p]revious studies" that concluded "measurement of 6-MP metabolic levels can be used to predict clinical efficacy and tolerance" to thiopurine drugs).[2]

What the Prometheus patents purport to add to the art is a recognition that *particular metabolite levels* correlate to proper drug dosages for certain gastrointestinal disorders. App., *infra*, 2a-3a; '623 Patent at 8:40-46, C.A. App. A10010. Those correlations already existed in the studied patient population; Prometheus simply looked at the data for that population to "discover" the levels. App., *infra*, 41a-42a; C.A. App. A12833-12836, A13330-13331.

Claim 46 of the '623 patent, for example, describes such a correlation review process. The sole step in that process involves recognizing the relevance of certain metabolite levels (known as 6-thioguanine (6-TD) or 6-methyl-mercaptopurine (6-MMP)):

> 46. A method of optimizing therapeutic efficacy and reducing toxicity associated with treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) determining the level of [6-TD] or [6-MMP] in a subject administered a drug selected from

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[2] See also '623 Patent at 9:13-14, C.A. App. A10011 (relevant metabolite levels "can be determined by methods well known in the art"); C.A. App. A12698-12701, A12705-12712, A12714-12718 (scientific papers from 1982-1990 describing tests for relevant metabolite of thiopurine); *id.* at A12722-12727 (1989 article discussing "acute thiopurine toxicity"); *id.* at A12842-12844 (conceding prior testing for thiopurine metabolites).

> the group consisting of 6-mercaptopurine, azathioprine, [6-TD], and [6-MMP], said subject having said immune-mediated gastrointestinal disorder;
>
> wherein the level of [6-TD] less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject, and
>
> wherein the level of [6-TD] greater than about 400 pmol per $8x10^8$ red blood cells or a level of [6-MMP] greater than about 7000 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

C.A. App. A10018; see App., *infra*, 3a-5a (describing patent claims at issue). With their technical terms stripped away, Prometheus's claims cover a physician's observation that a test result shows a metabolite level below 230, between 230 and 400, or above 400—*i.e.*, his mental recognition of a natural correlation between metabolite level and patient condition following administration of a drug. See App., *infra*, 3a.

Importantly, Prometheus's claims do not recite what is to be done once the physician recognizes the correlation. App., *infra*, 38a-39a. As a result, the claims cover and preempt *all* such uses. They begin and end with observation of the test results. What the physician might do with that observation is irrelevant because simply thinking about the subject suffices to infringe the patent. As Prometheus's expert testified, if the physician reads an email with the test results, it would not matter if 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." C.A. App. A13557-613558; see also C.A. Supp. App. A13805-13806. The physician infringes the moment she recognizes the correlation.

Prometheus confirmed the broad scope of its claims when it opposed Mayo's argument in the district court that the claims should be construed to require that physicians actually do something with their knowledge before they could be deemed to infringe—*e.g.*, adjust a dosage level for the patient. C.A. App. A12245-12249. Prometheus successfully argued that the physician would only have to identify a potential need to adjust dosage and denied that the physician must actually adjust the dosage or do anything else. See App., *infra*, 84a-86a.

The extraordinary breadth of Prometheus's patents is made evident by Prometheus's infringement accusations against Mayo researcher Dr. Rokea el-Azhary. Dr. el-Azhary is a dermatologist and therefore unconcerned with metabolite ranges for gastrointestinal disorders. She administered a thiopurine drug to her dermatological patients to see if she could *establish* a therapeutic range for skin disorders. See C.A. App. A12846. But because the lab report she received referred to the correlation ranges in Prometheus's claims, Prometheus accused Dr. el-Azhary of infringement:

> The Biochemical Genetics Laboratory at Mayo Clinic Rochester sent a report of test results to Dr. el-Azhary, or someone working for Dr. el-Azhary. The test results described the "therapeutic range" as "235-400." The Biochemical Genetics Laboratory at Mayo Clinic Rochester did not subsequently advise

> Dr. el-Azhary that the "therapeutic range" was not "235-400."
>
> Such information informed Dr. el-Azhary, or someone working for Dr. el-Azhary (and thus "indicated a need"), that the next dose of azathioprine given to the patient should be increased in order to be within the "therapeutic range."

C.A. App. A12788; A12821-12822. Prometheus even asserted infringement when Dr. el-Azhary subsequently received reports that did not list the "therapeutic range"—on the ground that the ranges were then in her memory. *Id.* at A12853-12854 ¶ 5.

Dr. el-Azhary testified that she knew the numbers, but that metabolite levels relevant to gastrointestinal conditions were "irrelevant to [her] study" because she was researching metabolite correlations in dermatology, not in inflammatory bowel disease, and "there is no reason to extrapolate to dermatology." C.A. App. A12848-12850. Under Prometheus's view of its patents, however, Dr. el-Azhary cannot resume her dermatological research unless and until she rids her memory of the correlations that Prometheus observed in gastrointestinal patients, regardless of how she ultimately may use any test results. She infringes whenever she recognizes the correlations, no matter what else she thinks or does.

In the courts below, Prometheus attempted to gloss over its accusation against Dr. el-Azhary by pointing out that it sued Mayo and not Dr. el-Azhary. But the el-Azhary episode dramatically highlights the broad range of medical research that Prometheus has preempted with its patents. By targeting Dr. el-

Azhary's thoughts, Prometheus can effectively stop her from determining appropriate ranges for her own dermatology patients, because she cannot definitively stop thinking about the metabolite correlations on which Prometheus's patents are based. Anyone who has read Prometheus's patent claims, or any summary of them—including readers of this petition—is similarly disabled. That Prometheus did not name Dr. el-Azhary as a defendant misses the point. If Prometheus were right that she has infringed its patents, any owner of a patent with similar claims could sue a physician in Dr. el-Azhary's position for infringement simply for thinking "forbidden" thoughts. The patent laws were never meant to impose such intolerable consequences.

B. The District Court's Decision Invalidating The Patents

In 2004, Prometheus filed a patent infringement claim against Mayo after Mayo developed and proposed to sell a test to measure metabolites in patients treated with thiopurine drugs that used different levels from those included in Prometheus's patents. App., *infra*, 61a-62a. Construing Prometheus's patent claims in accordance with their broad language, the district court granted Prometheus summary judgment on its infringement claim. *Id.* at 86a-93a.

After the district court permitted the parties to amend their pleadings, Mayo filed a motion for summary judgment contending that Prometheus's patents were invalid. The court granted Mayo's motion, at the same time denying Prometheus's motions for summary judgment on infringement and patent exhaustion. See App., *infra*, 28a-30a (describing procedural history).

In invalidating Prometheus's patent claims under 35 U.S.C. § 101, the district court relied on this Court's case law deeming patent claims invalid if they wholly preempt all uses of a natural phenomenon or abstract idea. App., *infra*, 36a-39a, 42a, 48a-54a. The court started by determining that the Prometheus claims recite correlations between thiopurine drug metabolite levels and therapeutic efficacy or toxicity. *Id.* at 38a-39a. The court rejected, as form over substance, Prometheus's argument that the claims recite "methods" rather than natural phenomena. Looking at the steps of the claims, the court explained that the steps reciting "administering" a drug and "determining" metabolite levels were mere data-gathering steps that were necessary precursors for reviewing the claimed correlation. *Id.* at 39a. In summarizing the claims, the court noted: "what the inventors claim to have discovered is that particular concentrations of [thiopurine metabolites] correlate with therapeutic efficacy and toxicity in patients taking AZA drugs." *Ibid.*

The court then ruled that the correlations are natural phenomena. Rejecting Prometheus's argument that the correlations could not be natural because thiopurine is a synthetic drug, the court observed that Prometheus's claims are directed to the correlation and not to the making of the drug. Prometheus's expert had admitted that "the key therapeutic aspect of such thiopurine drugs is that they are converted *naturally* by enzymes within the patient's body to form an agent that is therapeutically active." App., *infra*, 41a. Prometheus also admitted that the testing and correlations already existed in a "data-base of patient's information" that included patients taking 6-MP drugs, and that the correlations likely still exist in the current patient

population. *Ibid.* As a result, the court concluded (*id.* at 42a), Prometheus

> did not "create" the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity. Instead, the correlation results from a natural body process, which as the inventors concede, was pre-existing in the patient population, and it exists in the patient population today.

In analyzing Prometheus's claim, the district court found instructive the opinion of Justices Breyer, Stevens, and Souter in *LabCorp*. The district court quoted approvingly the *LabCorp* dissenters' explanation that the similar patent claim at issue there failed "the requirement that it not amount to a simple natural correlation, *i.e.*, a 'natural phenomenon'" (citing this Court's precedents):

> At most, respondents have simply described the natural law at issue in the abstract patent language of a "process." But they cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. One might, of course, reduce the "process" to a series of steps, *e.g.*, Step 1: gather data; Step 2: read a number; Step 3: compare the number with the norm; Step 4: act accordingly. But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable "natural phenomenon," and I

> can find nothing in [the claim] that adds anything more of significance.

LabCorp, 548 U.S. at 137-138 (citation omitted), quoted at App., *infra*, 43a-44a.

Finally, applying this Court's precedents to the record before it, the district court held that the Prometheus claims preempt a natural phenomenon. It first noted that the governing test was not a "transformation/results" test, because this Court had utilized a preemption test in *Gottshalk* v. *Benson*, 409 U.S. 63 (1972), and had invalidated a claim in *Parker* v. *Flook*, 437 U.S. 584 (1978), under the preemption rule without ever mentioning that test. App., *infra*, at 49a-50a. Then, applying the preemption rule, the court held that Prometheus's sweeping claims improperly preempt all uses of the correlations. *Id.* at 51a-54a. That ruling followed from the court's earlier determination that every other activity described in the claims, apart from recognition of the correlation, is a data gathering step necessary to make the correlation (*id.* at 51a):

> what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and/or toxicity in [patients] taking AZA drugs. Because the claims cover the correlations themselves, it follows that the claims "wholly pre-empt" the correlations.

C. The Federal Circuit's Decision Upholding The Patents

The Federal Circuit reversed. It glossed over Justice Breyer's *LabCorp* opinion in a footnote, describing it as non-binding but never dealing with its synthesis of controlling law. While noting that the

Prometheus claims addressed different blood tests from those in *LabCorp*, the court of appeals did not come to grips with the fact that *both* sets of claims purport to cover a mental correlation between patient metabolite levels and patient health.

Instead of applying this Court's "preemption" test, as the district court had done, the Federal Circuit applied its own "machine or transformation" test from *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), cert. granted, 129 S. Ct. 2735 (2009). The Federal Circuit began by calling its "machine or transformation" criterion a "definitive test," and ended by declaring that it replaces the preemption standard:

> [B]ecause the claims meet the machine-or-transformation test, they do not preempt a fundamental principle.

App., *infra*, 24a.

Prometheus invited that ruling by insisting in its briefing that "a freestanding preemption inquiry is inappropriate" because "*Bilski's* 'machine or transformation test is the singular test for a process claim under § 101.'" Prometheus Reply Br. at 21 n.3 (Fed. Cir. Apr. 24, 2009) (quoting *In re Ferguson*, 558 F.3d 1359, 1365 (Fed. Cir. 2009)). The Federal Circuit ultimately focused only on *Bilski* and its own "machine or transformation" test—mentioning this Court's decisions principally through citations to the *Bilski* opinion. App., *infra*, 9a-10a, 15a, 18a. Thus, the Federal Circuit has effectively rendered this Court's preemption test meaningless by making its own "machine or transformation" test controlling.

REASONS FOR GRANTING THE PETITION

By making its "machine or transformation" test the definitive test for patentability under Section 101, the Federal Circuit assumes that a process that involves a machine or transformation cannot possibly preempt all uses of a fundamental scientific principle. That ruling conflicts with this Court's precedents. This Court has utilized the preemption standard as a freestanding criterion, has found preemption without ever asking whether an invention involves a machine or transformation, and has deemed the presence of a machine or a transformation a mere "clue" to patentability. Like the claims in *LabCorp*, the Prometheus claims do not come close to escaping the preemption prohibition. The Federal Circuit's ruling should accordingly be reversed.

I. THE FEDERAL CIRCUIT'S ELEVATION OF ITS "MACHINE OR TRANSFORMATION" TEST TO THE SINGLE DETERMINANT OF PATENTABILITY CONFLICTS WITH THIS COURT'S PREEMPTION STANDARD.

A. The Court has long invalidated patent claims that attempt to preempt all uses of a natural phenomenon.

Although Section 101 is expansive in its reach—covering "anything under the sun that is made by man," *Diamond* v. *Chakrabarty*, 447 U.S. 303, 309 (1980)—it also is subject to important limits. In particular, a patent claim cannot preempt, either directly or by practical effect, a law of nature, natural phenomenon, or abstract scientific idea. As *Chakrabarty* observed:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable

> subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of * * * nature, free to all men and reserved exclusively to none.'

Id. at 309 (quoting *Funk Bros. Seed Co.* v. *Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). As the Court has also noted, "[p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk* v. *Benson*, 409 U.S. 63, 67 (1972).

This exception to patentability applies not only to a patent claim that is aimed directly at a natural phenomenon, but also to one whose "practical effect would be a patent on the [phenomenon] itself," because such a claim "wholly pre-empt[s]" all uses of the natural phenomenon. *Benson*, 409 U.S. at 71-72. Thus, where a claim recites a law of nature or biological principle, a court must look to whether the claim seeks protection for the phenomenon "in the abstract" or instead implements the phenomenon "in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect." *Diamond* v. *Diehr*, 450 U.S. 175, 191 (1981).

B. Prometheus's claims are invalid because they preempt all uses of the natural correlation between patient metabolite levels and patient health.

The Prometheus claims, like the *LabCorp* claims, recite a natural phenomenon—the correlation between certain metabolite levels and patient health.

That correlation is dictated by natural enzymatic activity inside the human body. As Prometheus's own expert admitted, the drugs are "converted *naturally* by enzymes within the patient's body" into metabolites, as the district court found. The Federal Circuit did not disturb that finding by the district court.

The Prometheus claims preempt all substantial uses of the correlations. In particular, the claims end with the step of recognizing the correlation, and thus cover *anything* that a physician might do with her knowledge of the correlation. Prometheus's expert confirmed the preemptive effect of the claims by testifying that a physician who receives test results that identify the claimed ranges will infringe regardless of what she does with the information—even if she crumples up the test result and throws it away, and regardless of whether or not she acts upon it. C.A. App. A13557-613558; see also C.A. Supp. App. A13805-13806.

The preemptive impact of Prometheus's claims is particularly severe because they are centered on human thought that involves, in any medical context, metabolite ranges that Prometheus observed in patients who took gastrointestinal drugs. Thus, dermatologist Dr. el-Azhary cannot stop thinking about Prometheus's ranges now that she knows of them, even if her goal in reviewing a patient's test results is to find entirely different numbers relating only to dermatology. As a result, Prometheus has obtained a monopoly in a very broad field of medical practice. The preemptive scope of the Prometheus claims is unprecedented. It constitutes an embargo on research and analysis essential to the development of medical knowledge and patient care.

This Court's decisions in *Benson*, *Flook*, and *Diehr* explain the governing preemption standard. In *Flook* and *Benson*, the claims were invalid because they recited a computation but not what was to be done with the computation, thereby covering all its uses. In *Diehr*, the claim recited both a computation of an algorithm and a real-world physical action to be performed with the computation, thus leaving open the possibility that others could make noninfringing uses of the computation. Because it was so limited, there was no preemption. The claims in *Benson* recited a computation for converting numbers from one form to another, but did not recite what was to be done with the numbers once they were converted. Hence, the patent covered all such uses of the idea and would wholly preempt the underlying mathematical formula. 409 U.S. at 71-72. In a like manner, the claims in *Flook* recited a process for updating an alarm limit for use in a chemical process, but never recited what was to be done with the computation even though the claims did recite some "post-solution activity." 437 U.S. at 590. Because the claims covered all uses, they, like the claims in *Benson*, were held invalid.

By contrast, the claims in *Diehr,* which recited use of the Arrhenius equation, also recited a particular application of the equation: using the output of the equation to determine when to open or close an injection mold. In distinguishing that situation from *Benson* and *Flook*, the Court explained (450 U.S. at 187) that

> respondents here do not seek to patent a mathematical formula. Instead, they seek patent protection for a process of curing synthetic rubber. Their process admittedly

> employs a well-known mathematical equation, but they do not seek to pre-empt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.

Prometheus's claims are like those in *Benson* and *Flook* and unlike those in *Diehr*. Claim 46, quoted above, involves nothing more than a physician's recognition of a natural correlation that is part and parcel of a patient's own natural metabolic processes. The claim is not limited to a particular real-world use of that recognition, such as requiring that the physician actually change the dosage after recognizing the correlation. Rather, the claim preempts *all* possible uses of the correlation and thus effectively monopolizes the natural correlation itself.

Prometheus's claims are invalid for the reasons set forth in the opinion of Justices Breyer, Stevens, and Souter in *LabCorp*. In *LabCorp*, the claims were directed to a method of "correlating" a blood homocysteine level with a deficiency in folate, just like the correlation between metabolites and patient condition in the Prometheus claims. Hence, "[t]here can be little doubt that the correlation [is] a 'natural phenomenon.'" 548 U.S. at 135. Like the claims in *LabCorp*, Prometheus's claims simply characterize the use of the correlation as a process, which was plainly insufficient in *LabCorp*:

> At most, respondents have simply described the natural law at issue in the abstract patent language of a "process." But they cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. * * *

> [H]ere, aside from the unpatented test, [the steps in the claim] embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable "natural phenomenon," and I can find nothing in [the claim] that adds anything more of significance.

Id. at 137-138. Prometheus's claims fail for the same reason.

Prometheus's central argument in the courts below was that thiopurine is a man-made, not natural, drug (whereas the drug in *LabCorp* was naturally occurring). But as the district court recognized, Prometheus's claims are directed to the correlation and not the drug itself (which Prometheus did not invent). And that correlation results from the body's natural metabolism of the drug. In short, Prometheus cannot take advantage of a drug that was invented by someone else, when its claims are exclusively directed to observing the human body's process of metabolizing the drug—a process that occurs naturally in the human body.

Granting patent protection here simply because Prometheus used a man-made drug would be inconsistent with this Court's invalidation of the patent claims in *Funk Bros.* There, the inventor discovered that certain bacteria could be isolated, mixed together so as not to inhibit each other's properties, and thereby serve as a crop inoculant. 333 U.S. at 130. The Court held the claims invalid because the inventor did not "create" the "state of inhibition or of non-inhibition in the bacteria," but instead "[t]heir qualities are the work of nature." *Ibid.* Of course the claimed combination of bacteria

was man-made. But the inventor had not created the natural phenomenon that was central to the invention. Likewise, Prometheus did not "create" any correlation between metabolite levels and drug efficacy or toxicity, because those correlations were pre-existing in the tested patients, have been observed and analyzed by physicians in their patients for decades, and exist today with or without Prometheus's patents.

In short, the Prometheus patent claims preempt a broad field of scientific thought and research. They seek to monopolize a scientific principle in a manner that is forbidden by this Court's patent preemption rulings. The Federal Circuit's decision conflicts with those rulings and should be reversed.

C. The Federal Circuit improperly applied its "machine or transformation" test in place of this Court's preemption standard.

The fundamental error in the Federal Circuit's resolution of this case was its replacement of this Court's "preemption" standard with its own "machine or transformation" test. As shown above, this ruling is at odds with settled precedent of this Court. In addition, the elevation of the rigid "machine or transformation" test to conclusive status is erroneous and exceptionally harmful.

First, although the Federal Circuit in *Bilski* claimed to find support for its test in this Court's decisions in *Benson*, *Diehr*, *Flook*, and *Cochrane* v. *Deener*, 94 U.S. 780 (1876), those opinions do not say that "machine or transformation" is a dispositive test for patentability or a substitute for the preemption standard. For example, the portion of *Benson* cited

by the Federal Circuit simply says that a transformation or reduction of an article to a different thing is "the clue" to patentability of a method claim that does not involve a particular machine. 409 U.S. at 70. A clue is a guide, not a definitive test.

In any event, the Prometheus claims do not result in any transformation. The only transformation cited by the Federal Circuit was a natural transformation that had already occurred in the patient population that Prometheus studied before it even looked at the test results. The transformation envisioned by *Benson* and other cases is a transformation that makes particular use of the natural phenomenon, and thus prevents the claim from preempting all possible uses. Likewise, the claims in *Diehr* were found patentable, not because a physical transformation was associated with them, but because the claims were limited to a narrow and particular use of the Ahhrenius equation—opening and closing a plastic mold. 450 U.S. at 187.

The Federal Circuit's decision draws even less support from the other two cases on which it relied in *Bilski*—*Flook* and *Cochrane*—because those cases make no mention of such a test. The *Flook* claims involved calculations performed using a computer (a machine) and included a transformation of an "alarm limit" that signaled the presence of abnormal conditions during catalytic conversion. 437 U.S. at 585-586. The Court nevertheless found the claims invalid because this transformation was insignificant "post-solution" activity that did not alter the fact that the claim was directed at a "mathematical formula" for updating alarm limits. *Id.* at 593-595. While the Court observed in a footnote that an "argument can be made" that the Court has affirmed

process claims only when the process "either was tied to a particular apparatus" or operated to change materials to a "different state or thing" (*id.* at 588 n.9), *Flook* did not adopt such a position. Even that possible "argument" made "machine or transformation" a minimum requirement, not a definitive test for patentability.

Likewise, in *Cochrane*, the Court simply noted that a process "is a mode of treatment of certain materials to produce a given result," and "an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing." 94 U.S. at 788. It did not identify either "machine" or "transformation" as a test, let alone *the* test, for patentability. By their omission of any "machine" or "transformation" analysis, these two cases confirm that "machine or transformation" is not the definitive standard for patentability under Section 101.

Shutting its eyes to this Court's preemption standard, the Federal Circuit observed that giving a drug to a patient was "'central to the purposes of the claimed process.'" App., *infra*, at 10a; see *id.* at 20a. But the court overlooked the fact that giving the drug was simply a preparatory data-gathering step for the ultimate correlation and did not limit the use of the correlation in any manner. The court also misperceived the relevance of any "transformation." If the transformation limits the claim to a particular real-world use of the fundamental principle, it can be supportive of patentability. But if it is merely a preparatory data-gathering step—leaving the rest of the claim open to preempt all uses of the principle—it does not make an otherwise unpatentable claim patentable. Thus, whether or not a patient receives a

thiopurine drug (a drug not invented by Prometheus), none of Prometheus's claims is limited in any manner: they cover anything done with knowledge of the natural correlation.

In the end, the "machine or transformation" test appears to be another effort by the Federal Circuit to fashion an inflexible standard that is unmoored from Congress's purposes in enacting the patent laws. This Court repeatedly has rebuffed such interpretations in recent years. For example, in *KSR Int'l Co.* v. *Teleflex, Inc.*, 550 U.S. 398, 418 (2007), the Court faulted the Federal Circuit for establishing an inflexible "teaching, suggestion or motivation to combine" standard that did not comport with the underlying rationale set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1 (1962), and other precedents. In *Medimmune, Inc.* v. *Genentech, Inc.*, 549 U.S. 118 (2007), the Court was critical of the Federal Circuit for adopting an inflexible rule for declaratory judgment jurisdiction, where that rule was unmoored from the underlying "case or controversy" requirement. And in *eBay Inc.* v. *MercExchange, L.L.C.*, 547 U.S. 388 (2006), the Court faulted the Federal Circuit for applying an inflexible injunction standard that did not address the full range of underlying equitable considerations. The Federal Circuit's adoption of a rigid "machine or transformation" standard here, which allows Prometheus to preempt a broad field of scientific thought and research, is equally indefensible.

II. CERTIORARI SHOULD BE GRANTED TO RESOLVE THE IMPORTANT QUESTION LEFT UNRESOLVED IN *LABCORP*.

The Court should grant review rather than hold the petition for *Bilski*. As the government empha-

sized in *Bilski*, that case turns on whether Bernard Bilski's invention is the sort of "technology" that should properly be protected by a patent. *E.g.*, U.S. Br. in *Bilski*, No. 08-964, at 8 (issue in *Bilski* is whether "methods of organizing human activity that are untethered to technology" are "technological and industrial processes" eligible for protection under Section 101). The resolution of that case will not decide the independent question raised here—whether an invention preempts a scientific idea by covering all uses.

This Court has already found the issue presented here to be certworthy in *LabCorp*. This case is an appropriate vehicle to resolve the important issue left undecided there for lack of issue preservation. The Prometheus invention is easy to understand and centered on a plain natural phenomenon. The Section 101 issue was the only issue raised on appeal, and it was addressed directly and extensively by the Federal Circuit and the district court. And because the Federal Circuit has exclusive jurisdiction over patent appeals from district courts (28 U.S.C. § 1295), erroneous decisions such as this one have immediate nationwide impact. Accordingly, this Court often grants review of Federal Circuit rulings based on the importance of the issue presented to the interpretation and application of the patent laws. *E.g.*, *Merck KGaA* v. *Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005). Such review is especially warranted here because the Federal Circuit's analytical error is fundamental and will be repeated if not corrected by this Court.

Furthermore, the question presented is one of extraordinary public importance at the heart of the patent laws. The critical need for this Court to

resolve that issue now is evidenced by the extensive amicus participation both in *LabCorp* and in the Federal Circuit in this case. Many amici stressed that patents like Prometheus's impede improvements in healthcare, drive up costs, and freeze innovation, as the dissenting Justices in *LabCorp* also recognized (548 U.S. at 138):

> [S]pecial public interest considerations reinforce my view that we should decide this case. To fail to do so threatens to leave the medical profession subject to the restrictions imposed by this individual patent and others of its kind. Those restrictions may inhibit doctors from using their best medical judgment; they may force doctors to spend unnecessary time and energy to enter into license agreements; they may divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations; they may raise the cost of health care while inhibiting its effective delivery.

These adverse consequences are profound given the sweep of the Federal Circuit's ruling and extend far beyond gastrointestinal disorders. If Prometheus can obtain a patent on correlations between drug administration and the resulting biological reactions in the human body, and prevent medical researchers and providers from thinking about those correlations in different ways, a host of medical entrepreneurs will claim patent monopolies on blood tests with the same preclusive consequences. A patent claimant could seek, for example, to monopolize the correlation between administration of anticoagulant drugs and chemical reactions in the blood, asserting that

these reactions are "man-made" phenomena, and thereby preclude improvements in this commonplace and essential form of medical care.

Therapeutic drug monitoring is fundamental to safely and effectively treating a variety of patient disorders with medication. Mayo, and physicians throughout the world, routinely measure metabolite levels in patients being treated with an array of drugs, including those for the treatment of epilepsy, heart arrhythmias, and depression. Therapeutic monitoring is also central to medicines used in the treatment of organ transplant and cancer patients. Improvements in the administration of all these life-saving drugs would be curtailed if patent claimants could assert a monopoly over every use of metabolite or other therapeutic correlations.

In this very case, Mayo sought to adjust the metabolite reference range deemed relevant by Prometheus to achieve more accurate results and improved patient care. App., *infra*, at 61a; Mayo Mem. in Support of Summary Judgment, filed Mar. 17, 2005, at 5-6 (Dkt. No. 15). But Prometheus blocked that innovation by asserting that it infringed Prometheus's exclusive right to specify relevant biological correlations.

The harmful impact of overly broad intellectual property protection on innovation is also of more general concern for the U.S. economy. Academic commentary confirms that allowing patents to preempt important fields, like medical diagnosis, by monopolizing scientific laws, would greatly increase costs and retard innovation. See M. Boldrin & D. Levine, AGAINST INTELLECTUAL MONOPOLY 73-77, 89-92, 184-187, 214-218, 238, 246 (2009) (describing dramatic increase in patent grants over last decade

resulting in a "patent thicket" harmful to innovation); L. Lessig, THE FUTURE OF IDEAS 205-217 (2001) (describing negative impact of broad patent protection on innovation; "we should be most concerned when existing interests use the legal system to protect themselves against innovation"); W. Landes & R. Posner, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 305-306 (2003) (patent monopolies on "scientific principles" threaten "enormous potential for rent seeking" and "enormous transaction costs that would be imposed on would-be users"); R. Merges & R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 915 (1990) ("[T]he real threat of a patent like this stems from the industry's close ties to science. * * * The Patent Office and courts should not permit the over-privatization of the scientific knowledge that makes the industry possible"); L. Branstetter, *Do Stronger Patents Induce More Local Innovation?*, 7 J. INT'L ECON. L. 359, 369 (2004) ("well-structured research projects conducted by competent scholars" have "failed to find" innovation benefits from expanded patent monopolies); A. Torrance & B. Tomlinson, *Patents and the Regress of Useful Arts*, 10 COLUM. SCI. & TECH. L. REV. 130, 138, 162-167 (2009) (collecting economic research showing lack of stimulus to innovation from broad patent grants).

At a minimum, and especially at this time of paramount national concern over health care costs and quality, this research shows "that a heavy burden of persuasion should be placed upon those who would extend such protection." S. Breyer, *The Uneasy Case for Copyright*, 84 HARV. L. REV. 281, 322-323 (1970) (citing research in patent and copyright fields). Prometheus has offered no such

justification for its sweeping monopoly on medical thought and research.

Beyond this, the decision below cannot be reconciled with the ethical duties of physicians. As explained in amicus briefs filed in the Federal Circuit by the American Medical Association and other medical organizations, patent protection of Prometheus's claims conflicts with ethical standards that require physicians to spread knowledge—and improve diagnostic criteria—for the benefit of mankind.

The Federal Circuit's decision also poses exceptional threats to First Amendment freedoms. Throughout our Nation's history, the freedom to think—to consider what one has seen, to reach mental conclusions based on those observations, and to change one's future plans in light of those conclusions—has been deemed sacrosanct. Reflecting that tradition, this court held in *Ashcroft* v. *Free Speech Coalition*, 535 U.S. 234, 253 (2002), that speech is generally protected from government restriction because "[t]he right to think is the beginning of freedom, and speech must be protected from the government because speech is the beginning of thought." Federal legislation, like the patent laws, must be construed to avoid conflict with First Amendment freedoms whenever possible. See, *e.g.*, *New York* v. *Ferber*, 458 U.S. 747, 769 n.24 (1982); ACLU Am. Br. in *Bilski*, No. 2007-1130 (Fed. Cir. Apr. 3, 2008), at 5-7, 14, available at http://www.aclu.org/pdfs/freespeech/in_re_bilski_aclu_amicus.pdf (a patent like that at issue in *LabCorp* amounts "to a patent on pure thought or pure speech"; courts "should interpret patent law doctrines * * * so as to

avoid difficult application of First Amendment doctrines").

Yet the decision below would make mere thought actionable under patent law and threaten sanctions including actual and treble damages. 35 U.S.C. § 284. Simply drawing a mental conclusion becomes, under the Federal Circuit's view, patent infringement, even without any further act. The infringement is complete when a doctor has recognized a correlation between the patient's metabolite levels and the patient's status, regardless of what the doctor may do based on such recognition. This cannot be the legal rule in a Nation committed to the First Amendment and to the tradition of freedom of thought.

At bottom, the Federal Circuit's ruling authorizes patents over the mere observation of natural phenomena. That ruling flouts this Court's precedents and the fundamental purpose of the patent laws. And it puts a stranglehold on innovation and progress in the vital field of medical diagnosis.

CONCLUSION

The petition for a writ of certiorari should be granted to resolve the issues left undecided in *LabCorp*. At a minimum, the petition should be granted, the decision below vacated, and the case remanded for reconsideration in light of this Court's decision in *Bilski*.

Respectfully submitted.

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