No. 12-398

IN THE

Supreme Court of the United States

THE ASSOCIATION FOR MOLECULAR PATHOLOGY, ET AL.,

Petitioners,

—v.—

MYRIAD GENETICS, INC., ET AL.,

Respondents.

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

REPLY BRIEF FOR PETITIONERS

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INTRODUCTION

Myriad identified two genes that exist in every person. It did not create, invent, or design the genes by "isolating" them. Its patents claim products and laws of nature and thus are invalid under Section 101.

Myriad does not dispute that BRCA gene fragments appear in the body, with covalent bonds broken and separated from material such as chromatin with which they are normally associated. Resp'ts Br. 51-52. It has thus essentially abandoned any defense of the insignificant structural differences asserted by the Federal Circuit majority. In addition, although Myriad emphasizes the use of genes as probes and primers, it concedes that the claims are not limited to probes or primers. *Id.* at 8, 42. What remain are Myriad's arguments that it extracted the genes from the body and added to the storehouse of knowledge. The first would not distinguish patenting a gene from patenting a kidney. The second is precisely rejected by the law or product of nature doctrine.

Myriad dismisses this Court's product and law of nature doctrine. It expands the Section 101 inquiry by repeatedly asserting that the difficulty of the task and the value of the result are relevant considerations. It contracts the inquiry by asserting that factors considered by this Court, such as whether what is patented has markedly different characteristics or preempts use of laws and products of nature, are irrelevant. Myriad also improperly places heavy reliance on the PTO's practice of granting gene patents. None of Myriad's arguments comports with this Court's precedents.

The assertions of Myriad's *amici* largely rest on the fear that a ruling in Petitioners' favor might prevent useful patents on tests, drugs, other DNA-related compositions such as recombinant DNA, or patents limited to particular uses. *See, e.g.*, Br. for Amici Curiae Genentech, Inc. et al. in Support of Resp'ts, Mar. 14, 2013 ("Genentech Br."). This case does not challenge the patent-eligibility of recombinant DNA (DNA that results from choosing fragments from genes or chromosomes that do not appear together in nature and stitching them together), recombinant therapeutic proteins, or genetically engineered antibodies. These patents are on naturally-occurring genes.

Finally, Myriad argues again that the case should be dismissed based on standing. That effort should be rejected.

ARGUMENT

I. ISOLATED DNA IS A PRODUCT AND LAW OF NATURE, NOT AN INVENTION.

A. DNA

Myriad has used four different arguments to explain why it believes "isolated" DNA is not a product or law of nature but instead its invention: isolated DNA has a different structure than DNA in the body, isolated DNA has a new function, isolated DNA is the result of extraction, and patents on isolated DNA add to scientific knowledge. None is persuasive; none establishes that Myriad designed, created, or invented the DNA.

Different Structure From DNA Found In Nature. Myriad argues that "isolated" DNA has a

different structure from DNA in the body. Resp'ts Br. 44. Myriad concedes that isolated DNA has the same nucleotides in the same order as genomic DNA and that isolated DNA conveys the same information and represents the same laws of nature as genomic DNA. *Id.* at 41. Myriad offers no specific structural alteration other than to refer to the structural differences identified by the Federal Circuit; *i.e.*, that in separating a gene from its chromosome, a covalent bond is broken. *Id.* at 42. Petitioners and *amici* have established that fragments of the BRCA genes with covalent bonds broken do exist in nature. Pet'rs Br. 10-11; Br. for Amicus Curiae Eric S. Lander in Support of Neither Party 12-18, Jan. 31, 2013 ("Lander Br."). Myriad does not dispute that. Resp'ts Br. 51-52. Because Myriad offers no other structural distinctions between "isolated" DNA and DNA, it has effectively conceded that none exists.

New Function. Myriad argues that "isolated" DNA can perform functions that DNA cannot perform.[1] Myriad is in effect arguing that it may obtain a patent on a product or law of nature itself if it finds a new use for it. Under this theory, Section 101 would not prohibit someone from obtaining a patent on gold if she found a new use for gold. As a matter of law, that argument is incorrect. *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289, 1293 (2012).

If one finds a new use for a product of nature, one may seek a method patent on that new use. Myriad, in fact, has claims to DNA for particular uses. *E.g.*, 2J.A. 823 (claim 16 of patent '282 on use

[1] Resp'ts Br. 7, 8, 35, 41-44.

of DNA as primer). Petitioners have not challenged those claims and the validity of such claims is not before the Court. The claims in this case are to the product of nature itself and not limited to any single use.

Myriad relies heavily on an argument that the patented genes acquire new functionality because they could potentially be used as probes or primers.[2] However, Myriad concedes that full-length genes, which are unquestionably included within its claims, cannot be used as primers. Resp'ts Br. 42. And Myriad concedes that none of the challenged claims is limited to the use of the DNA as a probe or primer, but instead reach any use. *Id.* at 8, 42. Thus, Myriad's alleged new functionalities do not justify the patent claim.[3]

Extraction.[4] Myriad argues that "isolated" DNA is different from DNA because it has been

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[2] The district court provided clear definitions of probes and primers. Pet. App. 264a-65a.

[3] Myriad only briefly alludes to its use of "isolated" DNA for purposes of diagnosis, perhaps because diagnosis is impossible if the isolated DNA is not identical to the DNA in the body. Moreover, "isolated DNA," standing alone, cannot diagnose cancer risk, Resp'ts Br. 42, n.12 – many more steps must be taken.

[4] Like the district court, petitioners use the term "extraction" rather than the term "isolation." Pet. App. 263a. Myriad has often used the term "isolation" to include both separation of the gene from the chromosome and also removal from the body. As noted above, Myriad did not refute that separation of the gene from the chromosome and other material such as chromatin does not distinguish "isolated" DNA from DNA. Accordingly, the only portion of the term "isolation" that is left is extraction from the body.

extracted from the body. Under this theory, Hans Dehmelt, who won the Nobel Prize for being the first to isolate a single electron from an atom, could have patented the electron itself. A kidney removed from the body (or gold extracted from a stream) would be patentable subject matter. Myriad's only response is to say that a kidney is an "organ" and DNA is not an "organ." Resp'ts Br. 56. But that distinction has no legal bearing. For the reasons stated more fully in Petitioners' opening brief, Pet'rs Br. 26-48, Myriad's patent claims to isolated DNA cover products and laws of nature and are therefore invalid.

Myriad's argument also fails to acknowledge that scientists have been extracting genes, including BRCA1 and BRCA2, from the body and other matter since at least the 1970's. Lander Br. 8 n.4 (explaining how fragments of the entire genome were extracted and collected).

Adding to the Storehouse of Knowledge. The only remaining argument that could support Myriad's patents is that Myriad added valuable information to the storehouse of knowledge. The cornerstone of the Section 101 doctrine, however, is that adding to the storehouse of knowledge is an insufficient basis for receiving a patent. *Funk Bros. Seed Co. v. Kalo Inoculant Co.,* 333 U.S. 127, 130 (1948); *Bilski v. Kappos*, 130 S. Ct. 3218, 3225 (2010); *Mayo*, 132 S. Ct. at 1301-02. Thus, the fact that Myriad scientifically annotated the genome by locating the particular nucleotides that form the BRCA genes does not satisfy Section 101.

Although Myriad claims an invention, the words it uses to most commonly describe its accomplishment are not about invention. The verbs

Myriad uses to describe its work are "identify," [5] "define,"[6] "locate,"[7] or "characterize."[8] Einstein "identified," "defined," and "characterized" the relationship between matter and energy, but his discovery was not patentable. *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). An astronomer who "identifies" or "locates" a new object in space and then "defines" or "characterizes" it as a comet has not turned that comet into her invention. The first scientists to isolate lithium from its naturally-occurring metallic form were not entitled to a patent on an element of the periodic table. Pet. App. 104a-05a.

B. The Expansiveness of Myriad's Claims Is Evidence of Their Ineligibility Under Section 101.

Myriad argues that a patent claim's scope is only relevant to the written description requirement of Section 112. But claim scope is directly relevant to many of the requirements of the Patent Act, including Sections 101, 102, and 103.

Myriad's claims reach the genes of every woman, man, and child in America. The moment any person's BRCA gene is removed, Myriad has exclusive rights to it even if Myriad never previously isolated DNA having that sequence and did not and could not know its sequence. The claims are expansive precisely because their bounds are defined

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[5] Resp'ts Br. 2, 6, 34, 38, 45.

[6] *Id.* at 2, 6, 7, 34, 38, 41, 43.

[7] *Id.* at 6.

[8] *Id.* at 34, 41, 42, 45.

by nature. The common link among the hundreds of millions of different compositions that are claimed is that they occur in nature and serve the functions dictated by nature. Likewise, the claims to any DNA coding for the BRCA protein and over any mutation that causes cancer are defined by nature. These are not claims written to specify particular DNA or cDNA that is used as a primer or probe to target particular genetic mutations, or that has been changed to produce a therapeutic protein. They are claims to products and laws of nature.

C. cDNA

1. The patent-eligibility of cDNA is not at issue in this case.

This case should be resolved without reaching the patent-eligibility of cDNA, because none of the claims is limited to only cDNA. For the first time, Myriad argues that some of its claims are so limited. Resp'ts Br. 11. This argument is inconsistent with the patents' language. The patents define DNA as used in the claims to include both DNA and cDNA. *See, e.g.*, Patent '282, 19:14-18, 19:51-53, 2J.A. 755.

Myriad argues that the compositions it now claims are limited to cDNA differ from genomic DNA because cDNA is "synthesized in laboratories and exclude certain regulatory and other non-protein-coding sequences (introns) found in native DNA and include only protein-coding DNA (exons)." Resp'ts Br. 12. Petitioners do not dispute that cDNA has these attributes; however, Myriad did not limit the cited claim (or any of the challenged claims here) to such attributes. In addition, the claims use the term "has" ("…wherein said DNA has the nucleotide

sequence…"). That term has a specialized meaning in patent law, generally interpreted to mean "including but not limited to." U.S. Patent and Trademark Office, Manual of Patent Examining Procedure § 2111.03, at 2100-45 (8th ed. Rev. 9 2012) (citing *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1573 (Fed. Cir. 1997) (applying the expansive meaning of the term to cDNA)).

Myriad attempts, nonetheless, to limit claim 2 of the '282 patent, 2J.A. 822, to these attributes by citing the "wherein" clause which references the sequence. Resp'ts. Br. 12. The "wherein" clause, however, does not reference any descriptive text adjoining the sequence. Thus, the only proper construction of claim 2 is that it covers "isolated DNA [with] the nucleotide sequence set forth." This language does not limit the claim to cDNA and covers any DNA that has the sequence given. To analogize, assume the patent claim at issue was to "an automobile of the color in figure X," which depicts a truck with red paint. Myriad would argue that the claim is limited to trucks with red paint, but the claim references only the color set forth in figure X, not the automobile type. If Myriad wanted to claim *cDNA* with the sequence that is described, it could (and should) have claimed "the cDNA molecule with the sequence…"

Finally, Myriad argues that claim 6 of the '282 patent, 2J.A. 822, is limited to cDNA. Resp'ts Br. 12. But claim 6 covers any nucleotide sequence containing 15 or more nucleotides from SEQ. ID NO:1, and 15 nucleotide (and longer) sequences from SEQ. ID NO:1 are found throughout genomic DNA. 1J.A. 631-34, 662-72; Pet. App. 114a-16a. *See also*

Jeffrey Rosenfeld & Christopher E. Mason, *Pervasive Sequence Patents Cover the Entire Human Genome*, 5 Genome Med. 27 (2013) (showing that 15-nucleotide sequences of BRCA1 match at least 689 other genes, that all human genes contain at least one patented 15-nucleotide sequence, and that current gene patents cover at least 41% of all known genes). To argue that claim 6 is limited to cDNA is simply to ignore its plain language and the facts.

2. If the Court concludes it must reach the issue of the patent-eligibility of cDNA, it should find cDNA unpatentable.

Myriad argues that because cDNA is generally made in a laboratory, it is patent-eligible. Resp'ts Br. 6-7. Petitioners anticipated and responded to this flawed argument. Pet'rs Br. 51-52.

The DNA that Myriad asserts is cDNA contains the identical genetic sequence as the coding regions in the naturally-occurring DNA of every person. 2J.A.755. The key difference between genomic DNA and cDNA is that the latter is complementary to natural mRNA, wherein the body has removed the non-coding regions. That removal occurs in the body by natural processes. Myriad has nothing to do with it. Pet'rs Br. 49-50.

In the laboratory, Myriad takes naturally-occurring mRNA from the body and simply relies on the natural binding properties of nucleotides to assemble the DNA. *Id.* Imagine the mRNA as magnets positively charged by nature. All that humans do is to add magnets negatively charged by nature (ordinary nucleotides). The nucleotide's

natural properties cause them to link and the result is called cDNA.[9]

cDNA is quite distinct from recombinant DNA, which is created when a geneticist selects cDNA or DNA fragments from different sources and intentionally stitches them together. Lander Br. 20. Any therapeutic application of cDNA requires further altering cDNA to create recombinant DNA. *Id.* But cDNA that simply mirrors naturally-occurring mRNA is a product of nature and a basic scientific tool; preempting its use impedes innovation. *See Mayo*, 132 S. Ct. at 1293.

II. MYRIAD ATTEMPTS TO SALVAGE ITS CLAIMS BY DISTORTING THE LEGAL STANDARD APPLICABLE TO SECTION 101, IN VIOLATION OF THIS COURT'S PRECEDENTS.

Myriad offers its own more expansive legal standard for Section 101: whether the composition is a result of "human intervention," emphasizing the degree of effort involved and the value of the products and laws of nature uncovered. Myriad also seeks to minimize factors identified by this Court such as preemption. Finally, Myriad deems dispositive that the Patent Office has approved of the compositions at issue. Resp'ts Br. 34, 49-50. Each of these arguments ignores, and in some instances rejects, the principles laid out in the Court's most relevant cases. *See, e.g.*, *Mayo*, 132 S. Ct. 1289;

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[9] The binding properties of nucleotides are not magnetic, but the qualities are analogous. It is thus inaccurate to say that Myriad "designed" or "created" either DNA or cDNA. Resp'ts Br. 6, 34.

Chakrabarty, 447 U.S. 303; *Funk Bros.,* 333 U.S. 127; *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931).

A. Invention Under Section 101 Cannot Be Reduced To Mere "Human Intervention."

In deciding whether a patent is valid under Section 101, the Court has not simply asked whether humans were involved in the purported invention, but instead examined the characteristics of what was patented and the extent to which the patent preempts use of a product or law of nature. *Mayo*, 132 S. Ct. at 1294; *Chakrabarty,* 447 U.S. at 308-10; *Funk Bros.,* 333 U.S. at 129-32; *American Fruit Growers*, 283 U.S. at 11-13. The Court has scrutinized whether the underlying product or law of nature has been transformed into something with a "distinctive name, character [and] use," and "markedly different characteristics from any found in nature." *Chakrabarty*, 447 U.S. at 309-10.

Myriad nonetheless argues that "markedly different characteristics from any found in nature" is not part of the legal analysis, Resp'ts Br. 40. *Compare with* Pet. App. 50a, 76a, 107a. Myriad further asserts that the Section 101 inquiry must focus on whether there are any differences between the patented composition and nature, no matter how overwhelming the similarities may be. Resp'ts Br. 40. As discussed in Section I, *supra*, the "differences" referred to by Myriad are unsupported by science or unspecified in the challenged patent claims. In any case, the Section 101 inquiry has never been limited in the manner Myriad now proposes. Under Myriad's view, the Court would have upheld the patents on

the *American Fruit Growers* fruit and the *Funk Brothers* bacteria; both were in some small measure different from the fruit and bacteria strains as they existed prior to the patentee's activity, but both were deemed unpatentable subject matter.

Instead of applying the Court's precedents, Myriad attempts to reduce the analysis to mere human intervention or human ingenuity. Defying more than 150 years of case law, Myriad states: "It is more judicious to determine patent-eligibility based on the presence of human ingenuity, rather than focus myopically on whether a natural law or product was somewhere involved." Resp'ts Br. 33.[10] But Section 101, as enforced by this Court, requires more than human ingenuity or intervention to establish patent-eligibility.

The electron, gold, and lithium examples illustrate this point: patent-eligibility does not rest on the difficulty or cost of defining the composition or on its value. *See Parker v. Flook*, 437 US 584, 593 (1978) (Section 101 determination must precede novelty and utility inquiries). Myriad highlights the praise it received after sequencing BRCA1 and BRCA2. Resp'ts Br. 5-6, 56-57.[11] The discovery

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[10] Myriad compounds its error by misconstruing *Chakrabarty*'s partial quotation of legislative history, Resp'ts Br. 16, without acknowledging that Congress clearly recognized the statutory limitations to patent-eligibility: "A person may have 'invented' a machine or a manufacture, which may include anything under the sun made by man, but it is not necessarily patentable under Section 101 unless the conditions of the title are fulfilled." H.R. Rep. No.1923, 82d Cong., 2d Sess., 6 (1952).

[11] Myriad fails to give due credit to the ground-breaking work of Dr. Mary-Claire King and her team, who identified the locus of the BRCA1 gene and similarly received wide acclaim. Kevin

deserves praise, but patents are not granted based on recognition, costs, or hard work. Incorporating such considerations into Section 101 would eviscerate this Court's long-standing precedent. Many compositions resulting from serious investment, such as drugs and new genetic technologies, deserve patent protection, but that is because they represent true inventions and not because resources were poured into their development.

B. Myriad's Patents Preempt Uses Of Laws And Products Of Nature.

The Court has made clear that patents cannot preempt all uses of any laws or products of nature or abstract ideas without running afoul of Section 101. *See Mayo,* 132 S. Ct. at 1293; *Bilski*, 130 S. Ct. at 3225; *Chakrabarty*, 447 U.S. at 313; *Funk Bros.,* 333 U.S. at 130-31; *O'Reilly v. Morse*, 56 U.S. 62, 113-18 (1853); Pet. Br. 40. The "preemption of nature" inquiry unearths the extent to which the patent interferes with using a law or product of nature. Myriad minimizes the relevance of preemption, even though "[t]he Court has repeatedly emphasized this last mentioned concern, a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature." *Mayo*, 132 S. Ct. at 1301.

Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* 2-6 (1996). The gene "came to be known as the 'BRCA1 gene,'" Resp'ts Br. 6, because Dr. King named it so. Others made significant contributions as well. *See, e.g.*, Kenneth J. Abel et al.*, A Radiation Hybrid Map of the BRCA1 Region of Chromosome 17q12-q21*, 17 Genomics 632 (1993).

All of the evidence presented in this case supports the conclusion that Myriad's patents preclude others' use of laws and products of nature. Because DNA must be isolated in order for clinicians and researchers to use the gene and the information it contains, the patents stop others from basic scientific activity. The patents are the reason why no other laboratory in the U.S. can conduct full sequencing of these genes, even using testing methods other than the one employed by Myriad. *E.g.*, Pet. App. 37a. The patents have been decried by famed geneticists like declarant John Sulston and *amici* James Watson and Eric Lander, all leaders of the Human Genome Project. *See* 1J.A. 129-40; Br. of James D. Watson Ph.D. as Amicus Curiae in Support of Neither Party 19, Jan. 31, 2013 ("Watson Br.") ("A human genome cluttered with no trespassing signs granted by the Patent Office inhibits scientific progress, particularly the development of useful tests and medicines in areas requiring multiple human genes"); Lander Br. 25 (these "claims erect an insurmountable barrier to studying these DNA sequences, with serious consequences for innovation in medicine"). They stand in the way of genetic testing companies like *amici* GeneDx and InVitae, which are among the many laboratories developing new technologies for sequencing human genes. *E.g.*, Br. of GeneDx and Law Professors as Amicus Curiae in Support of Pet'rs, Jan. 30, 2013; Br. of Amicus Curiae InVitae Corp. in Support of Pet'rs, Jan. 31, 2013. And they pose a serious barrier to developments in personalized medicine that could benefit us all. *E.g.*, Br. of Amici Curiae Am. Medical Ass'n et al. in Support of Pet'rs, Jan. 29, 2013 ("AMA Br."); Br. for Canavan Foundation et al. as Amici

Curiae in Support of Pet'rs, Jan. 31, 2013 ("Canavan Br."); Br. of AARP as Amicus Curiae in Support of Pet'rs, Jan. 31, 2013 ("AARP Br.").

Myriad attempts to refute this point by focusing on how it *chooses* to enforce its patents, not on the rights granted through the patents. Thus, it claims that because it has not enforced its patents against some scientists who engaged in research relating to the BRCA genes, there is no preemptive effect. Resp'ts Br. 48. Myriad may well decide not to sue certain researchers, particularly when their work may further knowledge about the genes and thus increase the value of Myriad's genetic testing services. But Myriad's argument ignores the authority it has and the documented chilling effect these patents have had as they influenced scientists' decisions about where to focus their work. 1J.A. 162-66, 219-24, 715-18; AARP Br. 3-6; Watson Br. 14, 16-22; Rosenfeld & Mason, *supra* at 5.

Myriad similarly asserts that whole genome sequencing or other sequencing methods would not violate its patents. That argument ignores the definition of "isolation" in its patents or as construed by the lower courts. Whole genome sequencing requires fragmenting DNA, including breaking its covalent bonds. Michael L. Metzker, *Sequencing Technologies – The Next Generation*, 11 Nature Reviews 31 (2010). The technician will inevitably "isolate" the BRCA1 and BRCA2 genes as she sequences the entire genome. Myriad cannot sidestep the fact that whole genome sequencing would violate its patents by claiming it would not enforce them against those testing methods (or not enforce it so long as the results are not shared with a patient, a

condition it has placed on researchers, *e.g.*, 1J.A. 59, 164, 171, 173, 186-97). *Cf.* Robert L. Green et al., Am. Coll. Med. Genetics, *ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing* 13, 25 (2013) (recommending that laboratories disclose BRCA genetic information when obtained incidentally through genome sequencing). The forbearance Myriad has expressed in this litigation offers no protection to any laboratory that wants to provide BRCA results as a part of a whole genome clinical assay. Similarly, Myriad refers to other testing methods that do not sequence DNA at all, but instead measure other biological phenomena such as gene expression. Because they do not involve the natural phenomena at issue here – a patient's BRCA genetic sequence – their existence is irrelevant to whether the patents preempt laws and products of nature.

C. PTO Practice Does Not Provide The Legal Framework To Decide The Question Presented.

Myriad further departs from this Court's precedent by arguing that PTO practice should be "an independent reason" to uphold patents under Section 101. Resp'ts Br. 28. PTO practice, however, has never been a decisive factor in determining patent-eligibility. *See, e.g.*, *Mayo*, 132 S. Ct. at 1304-05 (disapproving patents granted by PTO); *Chakrabarty,* 447 U.S. at 306 (upholding patents rejected by PTO). Indeed, the PTO routinely granted patents similar to the ones this Court found invalid in *Mayo*. Following this Court's ruling, the PTO issued two guidance documents to its examiners to

inform them how *Mayo* should change their patent-eligibility determinations. Andrew H. Hirshfeld, U.S. Patent & Trademark Office, *Preliminary Guidance to Patent Examining Corps on Supreme Court Decision in* Mayo Collaborative Services v. Prometheus Laboratories, Inc. (2012); Andrew H. Hirshfeld, U.S. Patent & Trademark Office, *Memo to Patent Examining Corps on 2012 Interim Procedure for Subject Matter Eligibility Analysis of Process Claims Involving Laws of Nature* (2012) ("Interim Procedure"). For example, the PTO noted that contrary to prior PTO practice, *Mayo* treated the correlation between metabolite levels, resulting from the administration of a drug, and drug efficacy as a law of nature. Interim Procedure at 7, n.5. The PTO further predicted that "[a]dditional guidance from the courts on how to identify laws of nature may be forthcoming in cases like *Myriad*." *Id.* Thus, the PTO, industry, and relevant stakeholders understand and expect that the courts have an important role in resolving Section 101 questions.

The legal framework for deciding patent eligibility is Section 101 and this Court's precedents. As the United States explains in its brief, the PTO's Utility Guidelines do not have the force of law. U.S. Br. 27-28. And contrary to Myriad's representations, Resp'ts Br. 29, the PTO has never taken a blanket position approving the patent-eligibility of isolated natural products. Indeed, the 1889 case of *Ex Parte Latimer* illustrates how the government recognized early on the dangers of allowing such patents. 1889 Dec. Comm'r Pat. 123 (1889). The Commissioner of Patents found that even though the fibers at issue were obtained by freeing them from the pine needle and removing extraneous matter, and thus made

more useful for mankind, they were not patentable. To rule otherwise would mean that "patents might be obtained upon the trees of the forest and the plants of the earth, which of course would be unreasonable and impossible." *Id.* at 126.

The issue of isolated DNA's patent-eligibility was not presented before any court until this case. The lower court decisions cited by Myriad, Resp'ts Br. 4-5, did not involve Section 101 or dealt with *purified* (referring to concentrated) compositions that were transformed to serve new functions, such as triggering therapeutic response; the patents therefore did not preempt examining or measuring the product of nature itself. Likewise, the legislative history that Myriad and its *amici* point to does not support upholding these patents. Congressional inaction on isolated DNA cannot support an inference that Congress endorsed the PTO's practice of issuing these DNA patents. *Rapanos v. United States*, 547 U.S. 715, 750 (2006) (plurality opinion); *Solid Waste Agency v. U.S. Army Corps of Eng'rs*, 531 U.S. 159, 169-70 (2001). *Cf. J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.,* 534 U.S. 124, 145 (2001) (referring to congressional enactment of legislation confirming that plants are patentable).[12]

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[12] Similarly, Myriad's references to international law are inapposite. The Agreement on Trade-Related Aspects of Intellectual Property ("TRIPS") allows governments to exclude patents on the grounds of public interest, the patent systems in other countries vary widely, and most allow for greater research than is permitted in the U.S.. TRIPS, art. 27; *Cancer Voices Australia v. Myriad Genetics Inc.* (2013) FCA 65 (Austl.) (court decision based on Australian patent law, which is "quite different" from American law); 1J.A. 699-702. Myriad does not have the same rights to BRCA in other countries. *See, e.g.*,

III. A RULING FOR PETITIONERS WILL HAVE POSITIVE RESULTS FOR INDUSTRY AND PATIENTS.

This Court has frequently said that patents on products or laws of nature can have severely negative effects on the advancement of science. *E.g.*, *Mayo*, 132 S. Ct. at 1293 ("monopolization of those tools through the grant of a patent might tend to impede innovation more than it would tend to promote it"). There is ample support in the record for that conclusion with regard to DNA. *See, e.g.,* 1J.A. 695-710; Pet'rs Br. 42-48. The claims also have had devastating effects on patients. Pet'rs Br. 7-9. *See*, *e.g.*, AMA Br. 6-13; Lander Br. 23-26; 29; Canavan Br. 10-16.

Myriad's *amici* do not seriously dispute these facts. Instead, they voice concern that a ruling for Petitioners might prevent patents on things other than "isolated DNA." For example, some fear that the Court's decision might reach patents on recombinant DNA. *See* Genentech Br. 4-5. Recombinant DNA is DNA in which the scientist has joined two or more DNA sequences that are not found together in nature in order to achieve certain effects. The recombinant DNA sequence and function are designed by the scientist, as opposed to the DNA in this case, where both the sequence and function are determined by nature. As many of the *amici* acknowledge,

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1J.A. 136-37, 213-14; Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing*, 10 Health L.J. 123, 143 (2002) (in Europe and Canada, Myriad was either unsuccessful in obtaining the broad rights granted in the U.S. or its patents were disregarded by the government).

recombinant DNA is the "invention" that enables the production of the novel proteins used to treat many diseases, and most economically valuable patents in the biotechnology industry are on recombinant DNA. *See id.* at 6-7; Lander Br. 20; Watson Br. 18, 21.

A ruling for Petitioners in this case would not preclude patenting of recombinant DNA. Petitioners' arguments pertain only to "isolated DNA," which is required to diagnose an individual's own genetic susceptibility to cancer and other conditions. Indeed, Myriad's BRCA1 and BRCA2 patents, particularly claims 5 and 6 of patent '282, 2J.A. 822, preclude all others from using BRCA1 or BRCA2 fragments to create recombinant DNA. Thus, a ruling for Petitioners would not jeopardize patents on recombinant DNA and would in fact facilitate that option.

Some of Myriad's *amici* express concern about the ruling's effects on the development of therapeutic drugs. First, it should be noted that this case does not challenge patents on drugs. Myriad did not develop a new drug and did not go through FDA trials or approval prior to offering testing. *See* Frederic M. Scherer, *The Economics of Human Gene Patents*, 77 Acad. Med. 1348, 1351-52 (2002) (biotechnology industry's profits and expenses relate to drug sales and FDA approvals, not genetic testing). Second, to the extent that *amici* argue that patenting isolated DNA was the first step toward their eventual development of drugs (and thus such patents must be upheld), the contention either seeks special treatment for biological products of nature, a proposition this Court recently rebuffed, or completely rejects the constitutional underpinnings

of the product and law of nature doctrine. *Mayo*, 132 S. Ct. at 1305. Locking up a product of nature such as two human genes through patents might very well benefit the patentholder, but at the expense of forcing the public to rely on a single entity to fully investigate the wide range of scientific, medical, and commercial potential for those genes.

To the extent Myriad or its *amici* are arguing that the patents in this case were necessary to create an incentive to search for the BRCA1 and BRCA2 genes or to commercialize a test for the genes, the record is clear that they were not. 1J.A. 244-60. Other scientists, including those who did not want patent exclusivity, were looking equally vigorously for the genes, *id.* at 136-38, 248-50, and other laboratories had begun testing for mutations until Myriad forced them to stop. Pet. App. 21a-22a, 37a. Myriad's monopoly on the BRCA genes has allowed it to dictate the quality and provision of BRCA genetic testing and to control the scientific knowledge about the genes, thereby limiting medical practice, chilling research, and restricting access to information crucial to women's health.[13] Patent protection at the

[13] Myriad's *amici*'s arguments that the claims' harmful effects could be ameliorated are based on speculation, rather than the law, as evidenced by the enforcement of the BRCA patents. There is no compulsory licensing regime, and compulsory licenses have never been ordered following *eBay, Inc. v. MercExchange, L.L.C.*, 547 U.S. 388 (2006). Similarly, the government has never exercised march-in rights over patents in which it has an interest. And the "research exception" to patent infringement is extremely narrow. *Madey v. Duke Univ.*, 307 F.3d 1351 (Fed. Cir. 2002) (noting any activity in furtherance of "legitimate business," regardless of profit motive, falls outside the exception).

level of the gene (versus on actual tests, recombinant DNA, etc.) is simply unnecessary to spur innovation in diagnostics. Rep. of the Sec'y's Advisory Comm. on Genetics, Health, and Soc'y, *Gene Patents and Licensing Practices and their Impact on Patient Access to Genetic Tests* 31 (Apr. 2010). In other contexts, gene patents have *interfered* with the availability of testing. AMA Br. 10.

A ruling for Petitioners in this case would not preclude patenting of recombinant DNA, new drugs, or new methods of diagnosis and/or treatment. Instead, it would ensure that human genes – the blueprint for human biology – can be accessed by all scientists and medical professionals working in diagnostics, biotechnology, pharmaceuticals, and other fields.[14]

IV. PETITIONERS HAVE STANDING.

For the fifth time in this case, Myriad argues that Dr. Ostrer does not have standing. Resp'ts Br. 17-22. The Federal Circuit formally rejected the argument three times. Pet. App. 25a, n. 6, 32a, 40a-42a. In twice granting the Petition in this case, this Court at least implied that it found the argument unpersuasive. The Court should reject it.

The Federal Circuit specifically found that:

- Myriad threated to sue Dr. Ostrer. *Id.* at 33a-34a.

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[14] As noted, Petitioners have not challenged claims limited to the use of DNA as a probe or primer. Section I, *supra*. Similarly, Petitioners have not challenged claims limited to diagnostic kits. *See, e.g.,* 2J.A. 823, cl. 18.

- Dr. Ostrer seeks to engage in infringing activities, *id.* at 32a-33a, and Dr. Ostrer "states unequivocally that he will immediately begin such testing . . ." *Id.* at 36a.
- Dr. Ostrer "has the resources and expertise to immediately undertake clinical BRCA testing. . ." *Id.* at 35a-36a.
- "Myriad's active enforcement of its patent rights forced Dr. Ostrer, as well as every other similarly situated researcher and institution to cease performing the challenged BRCA testing services . . ." *Id.* at 37a.
- "[T]he relevant circumstances surrounding Myriad's assertion of its patent rights have not changed despite the passage of time," *id.* at 36a, "Myriad and Ostrer have not altered their respective positions," *id.* at 37a, and "nothing in the record suggests that any researcher or institution has successfully attempted to compete with Myriad, or that Myriad has in any way changed its position with regard to its patent rights." *Id.* at 37a.

Given these facts, Dr. Ostrer clearly has standing. *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118 (2007). Myriad's argument – that no one has standing unless Myriad has recently and personally threatened them with suit for

infringement – is inconsistent with this Court's standing jurisprudence. *See* Cert. Pet. 32-35.[15]

CONCLUSION

For the foregoing reasons, the patent claims should be held invalid.

Respectfully submitted,

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[15] The Federal Circuit did find that the other petitioners lacked standing, Pet. App. 41a, and this Court denied certiorari on that issue.