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

BRIEF FOR THE PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA AS *AMICUS CURIAE* SUPPORTING RESPONDENTS

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March 14, 2013

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INTEREST OF AMICUS CURIAE

The Pharmaceutical Research and Manufacturers of America (PhRMA) is a voluntary, nonprofit association representing the nation's leading research-based pharmaceutical and biotechnology companies, which are the primary source of the many new drugs and biologics introduced each year. [1] *See* PHRMA MEMBER COMPANIES, *at* http://www.phrma.org/about/member-companies (last visited March 13, 2013).

There is significant diagnostic, therapeutic, and commercial value in isolated and purified biological materials. Innovators such as PhRMA's members are at the forefront of the breakthroughs involving these materials. In 2011 alone, PhRMA members invested nearly $50 billion in researching and developing new medications and vaccines that help patients live longer, healthier and more productive lives. *See* 2012 PHARM. INDUS. PROFILE, *at* http://www.phrma.org/sites/default/files/159/phrma_industry_profile.pdf (last visited March 13, 2013).

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[1] Pursuant to this Court's Rule 37.6, *amicus* affirms that no counsel for any party authored this brief in whole or in part, that no party or counsel for a party made a monetary contribution intended to fund the preparation or submission of this brief, and that no person other than amicus or its counsel made a monetary contribution intended to fund the preparation or submission of this brief. The parties have consented in writing to the filing of this brief.

In light of the great uncertainties and risks inherent in the development of medicines, PhRMA's members depend on a degree of certainty and predictability in patent law. For decades, PhRMA's members have invested in biotech research and development based on an assurance of the availability of patent exclusivity. In making investment decisions, PhRMA's members have relied upon a statutory framework that provides broad patent eligibility, decades of jurisprudence granting patent protection to isolated and purified biological materials (including isolated DNA molecules), and the USPTO's longstanding policy and practice. Accordingly, PhRMA urges the Court to uphold the settled expectations of innovators and clarify that although genes as they exist in the human body are not patent-eligible, "isolated" genes result from human intervention and ingenuity and thus are patent-eligible.

SUMMARY OF ARGUMENT

1. Human genes as they exist in the body are not patentable. But the patents at issue do not claim human genes as they exist in the body. Instead, the patents at issue claim isolated DNA molecules. This is a critical distinction. Although "native" genes and "isolated" DNA molecules both contain informational content capable of encoding a BRCA1/BRCA2 polypeptide, the similarities end there. Native genes exist as an unknown part of a complex host organism genome, embedded in much larger genomic sequences and surrounded by other cellular components. Extensive human intervention is

required to isolate specific DNA molecules from this complex matrix. Each claimed isolated DNA molecule is a tangible, human-made chemical compound that differs in structure, function, utility, and informational content from its native counterpart. Therefore, none of the patent claims at issue in this case read on genes as they exist in the human body.

2. Patent owners making research and development investment decisions have long relied on a statutory framework that provides broad patent eligibility, decades of jurisprudence recognizing isolated and purified biological materials as patent-eligible subject matter, and the USPTO's longstanding policy and practice with respect to those inventions. These settled expectations and substantial property rights should not be ignored. The discovery and development of new drug therapies and diagnostic tools is crucial to public health. The protections afforded by the federal patent laws are central to providing appropriate incentives to overcome the staggering costs and risks of developing new products and therapies.

3. Patent protection provides innovators with a limited period of exclusivity in order to encourage them to incur these enormous up-front costs and risks. In the pharmaceutical field in particular, because patent filings must be made years in advance of regulatory approval, research and development investment decisions necessarily depend on a degree of certainty and predictability in patent law—including certainty that the fruits of such research endeavors are patent-eligible.

The strength of the U.S. patent system depends upon the carefully calibrated balance of protecting and rewarding ingenuity in exchange for public disclosure. It is essential to provide appropriate incentives for continued innovation, particularly in the field of biotechnology. Over the past several decades, Congress has witnessed the USPTO grant thousands of patents claiming isolated DNA sequences and has opted to maintain the patent eligibility of these inventions. Because Congress is responsible for enacting legislation to "promote the progress of science and useful arts," the Petitioner's policy-driven arguments should be addressed to Congress, not to this Court.

ARGUMENT

I. Native Genes and Isolated DNA Molecules Are Fundamentally Different.

A. Native Genes Exist as Part of a Complex Host Organism Genome.

Living organisms contain genes composed of deoxyribonucleic acid (DNA). BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL 191 (4th ed. 2002) ("*Molecular Biology*"). These genes encode inherited genetic information and play a critical role in organism function. *Id.* More specifically, genes specify, or encode, peptide chains of amino acids that form proteins, which are the building blocks of living organisms and perform a vast array of functions, including catalyzing metabolic reactions, responding to stimuli, and even regulating the expression of other genes. *Id.* at 198. Native genes exist as an

unknown part of a complex host organism genome, embedded in much larger genomic sequences and surrounded by other cellular components. *Id.* at 207. Genes fulfilling particular functions are often given specific names, such as BRCA1/BRCA2 genes.

The human genome is composed of DNA. DNA as it exists in the human body (genomic DNA) is packaged into chromatin, which, in turn, forms chromosomes—long strands of DNA that contain many genes—and are associated with various proteins called histones. *Id.* Histones and other chromatin proteins define the conformation of the chromatin—information arguably as important in gene expression as the underlying DNA sequence itself. *Id.* at 207-08. A human being has twenty-three chromosome pairs, a full copy of which is contained in most human cells. *Id.* at 198.

The basic building blocks of DNA are repeating units of four nucleotide bases (adenine (A), thymine (T), cytosine (C), and guanine (G)), linked together via a phosphate sugar backbone. *Id.* at 193. In living organisms, DNA consists of two paired, but separate, DNA strands that form a double helix. *Id.* at 193-94. Generally, one of the strands is a "coding strand," and the other is a complementary "template" strand. *Id.* at 195-96. For example, the A on one strand pairs with the T of the complementary strand, the C on one strand pairs with the G of the complementary strand; and vice versa. The specific order of nucleotide bases that form a DNA strand is often referred to as a DNA sequence or gene sequence. *Id.* at 196.

Native DNA sequences contain both coding regions ("exons") and non-coding regions ("introns").

Id. at 202. These exons and introns are important to the creation of a protein from a DNA sequence. *Id.* at 317. In native DNA, introns represent the vast majority of a DNA sequence. *Id.*

At a basic level, protein creation results from two iterative processes, called transcription and translation. *Id.* at 302. Transcription is the process by which the information in the DNA sequence is transferred to a ribonucleic acid sequence. *Id.* Ribonucleic acid or RNA, is another nucleic acid in the body. *Id.* Similar in many respects to DNA, RNA is composed of four nucleotide building blocks, three of which (A, C, and G) are the same as DNA. *Id.* RNA however uses uracil (U) instead of the T in DNA. *Id.* These nucleotide building blocks are held together by a sugar phosphate backbone similar to the one used in DNA. *Id.*

When transcription begins, the DNA double helix is unwound, and the template DNA strand forms the template for the creation of a complementary RNA strand. *Id.* at 303. This RNA strand has the same sequence as the coding DNA strand, except that any Ts in the DNA sequence of the coding DNA strand are replaced by Us in the RNA sequence. Once this RNA sequence is created, the intron coding sections are removed, and the remaining exon sections are spliced together to create "messenger RNA" or mRNA. *Id.* at 317. Figure 1, below, demonstrates this process.

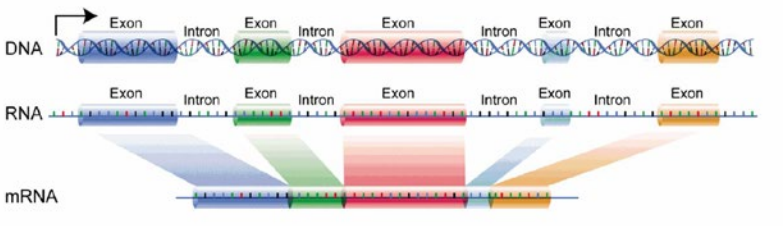

Figure 1

National Human Genome Research Institute *available at* http://www.genome.gov/Images/EdKit/bio2i_large.gif (last accessed March 13, 2013).

Translation occurs when the mRNA is used to create a particular protein. *Molecular Biology*, at 336. Proteins are made up of amino acids, which correspond to particular three-nucleotide combinations found in the mRNA. *Id.* These combinations are called codons. For example, the three-nucleotide combination CGU codes for the amino acid arginine. *Id.* There are sixty-four possible codons, which code for the twenty natural amino acids; certain codons also signal where the protein should start and stop. *Id.* Figure 2 below demonstrates how a particular mRNA strand (top) is translated into a particular peptide, comprised of specific amino acids (bottom).

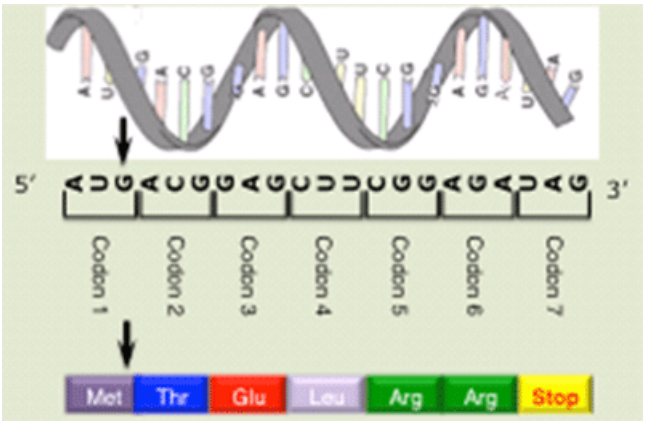

Figure 2

Professor Elizabeth Greyhack Lab, University of Rochester, *available at* http://www.urmc.rochester.edu/labs/Grayhack-Lab/images/geneticcode.png (last accessed March 13, 2013).

Mutations in the native DNA sequence can be extremely problematic. For example, a single nucleotide mutation can lead to the mis-coding of a single amino acid in a particular peptide. Even more serious mutations involve whole portions of a DNA sequence being deleted, rearranged or duplicated, which, in turn, leads to the potential loss or misplacement of particular genes and, accordingly, the proteins for which those genes code. *Molecular Biology,* at 454. Some of these mutations cause a particular disease, or lead to an increased risk of disease.

B. Isolated DNA Molecules and Native DNA Differ in Structure, Function, Utility, and Informational Content.

1. The Claimed BRCA1/BRCA2 Genes Are Distinct From the Section of Native DNA That Encodes the Same Proteins.

DNA as it exists in the human body and isolated DNA molecules differ in significant ways. For example, an isolated DNA sequence can be synthesized from the nucleotide building blocks in a lab. One of the most common forms of this type of isolated DNA molecule is complementary DNA, or cDNA. cDNA is made from a corresponding mRNA template, and therefore lacks many of the intron sequences found in a native gene sequence. For example, some of the claimed BRCA1/BRCA2 sequences, which are cDNA, omit certain non-coding introns (which in some genes account for more than 90 percent of the native gene's length). *See, e.g.*, U.S. Patent No. 5,747,282 (the "'282 patent"), cl. 2 (to 5.9 kb cDNA sequence, which is 1/10th the length of the native BRCA1).

Moreover, a native gene sequence may code for more than one protein. For instance, the longer native BRCA1/BRCA2 genes may be subject to alternative splicing, and thus may code for multiple proteins. *See* Miao Lixia et al., *Alternative Splicing of Breast Cancer Associated Gene BRCA1 from Cancer Cell Line*, J. BIOCHEM. AND MOLECULAR BIO. 15-21 (2007); Ivan Bieche et al., *Increased Level of Exon 12 Alternatively Spliced BRCA2 Transcripts in Tumor Breast Tissue Compared with Normal Tissue*,

J. CANCER RES. 2546-2550 (1999). In contrast, each of the claimed BRCA1 and BRCA2 sequences encode a single protein; again, rendering them distinct from their native counterparts.

2. The Process of Creating Isolated DNA Molecules is Complex and Results in a Chemically Distinct Molecule Relative to their Native Counterparts.

The isolation of DNA is a complex endeavor because DNA is not divided neatly into individual genes. As discussed above, native DNA exists in chromosomes, which are composed of chromatin surrounded by histones. Figure 3, below shows genomic DNA broken down into its component parts. Unlike gold that has been isolated from a stream or a leaf that has been snapped from a tree, these histones are part of, and integral to, the chromatin structure, and therefore, the DNA structure. The removal of this cellular material functionally and structurally alters genomic DNA.

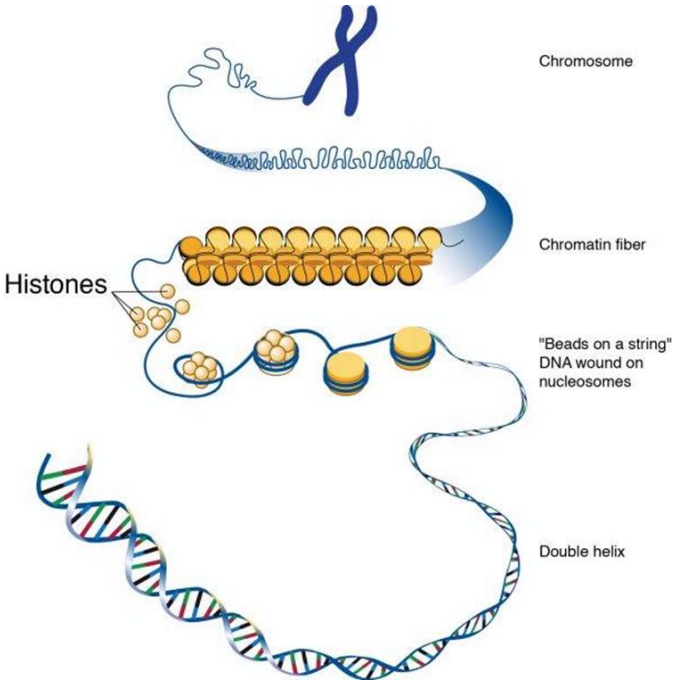

Figure 3

National Human Genome Research Institute *available at* http://www.genome.gov/dmd/img.cfm?node=Photos/Graphics&id=85183 (last accessed March 13, 2013).

When genomic DNA is extracted from a living cell, the DNA strand contains multiple genes that are attached to one another, end to end. Locating and excising a particular gene sequence from this genomic DNA is an iterative, complex process that requires specialized knowledge of the gene's composition. After being excised from the genomic DNA, isolated genes are no longer attached to other genes. These isolated genes, like the claimed isolated BRCA1/BRCA2 gene sequences, have free ends. Those free ends do not exist in nature, but are

necessary for biotech applications such as end labeling and primer extension, which are important tools in genetic engineering. *Molecular Biology*, at 207, 215–16, 222, 495, 508–09.

Explained another way, isolating a particular DNA molecule is a method of manufacturing that requires two forms of human intervention. First, when extracting the DNA, human intervention is required to physically destroy the cell by rupturing the cell membrane. Second, purifying the extracted DNA molecule requires human intervention to not only remove the material associated with the genomic DNA, but also to excise the particular isolated DNA molecule sought. *See, e.g.*, *Cancer Voices Australia v Myriad Genetics Inc.* [2013] FCA 65, ¶108 (Austr.). These steps result in what is in effect a type of manufactured product.

When isolated, DNA molecules are cleaved from their surrounding cellular material and in the process, they are chemically and functionally altered. This is because the isolated DNA molecule contains the information necessary, but not sufficient, for protein creation. In other words, the process of isolating a DNA molecule results in a distinct chemical entity with distinct attributes as compared to its native counterpart. Contrary to the Petitioner's suggestion, an isolated DNA sequence cannot simply be reinserted into the cell and function as it did previously.

In sum, the claimed isolated DNA sequences do not exist in nature; they are created in a laboratory. Because the claimed isolated DNA sequences are a product of human ingenuity, they are patent-eligible. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).

II. Myriad's Patents Are Directed to Patent-Eligible Subject Matter.

A. Human Genes Differ from the Claimed Isolated DNA Molecules, and Are Not Patentable.

Human genes, as they exist in the human body, are not patent eligible. But the patents at issue in this case do not claim human genes as they exist in the human body. Rather, certain patent claims at issue are directed to "isolated" DNA molecules encoding BRCA1/BRCA2 polypeptides and related diagnostic and therapeutic methods. As defined by the patentee, the invention is limited to DNA that "has been removed from its naturally occurring environment." *See* '282 patent, col. 19, lines 8-19.

The claimed isolated DNA molecules differ in "name, characteristics, and use" from their native counterparts and, as such, constitute patent-eligible subject matter. *Chakrabarty*, 447 U.S. at 309-310 (holding that the claimed invention was "a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use'").[2]

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[2] Although this brief will focus on the issue of patent eligibility, PhRMA agrees with the Respondents that the Petitioners lack standing.

B. Isolated DNA Sequences Fall Within the Broad Realm of Patent-Eligible Subject Matter.

Section 101 defines the subject matter that may be patented under the Patent Act as "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof . . . subject to the conditions and requirements of this title." 35 U.S.C. § 101. Congress adopted this expansive definition by design, recognizing that "ingenuity should receive a liberal encouragement." *Chakrabarty*, 447 U.S. at 308-309 (quoting 5 Writings of Thomas Jefferson 75-76 (H. Washington ed. 1871)). Only the laws of nature, physical phenomena, and abstract ideas have been carved out as exceptions. *Bilski v. Kappos*, 561 U.S. ___, 130 S. Ct. 3218, 3225 (2010); *Chakrabarty*, 447 U.S. at 309. Section 101 is a "dynamic provision designed to encompass new and unforeseen inventions." *Bilski*, 130 S. Ct. at 3227 (quoting *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.*, 534 U.S. 124, 135 (2001)).

Advances in the field of biotechnology fall squarely within the broad realm of "new and unforeseen inventions" contemplated by § 101. Nothing in the patent statute precludes the issuance of a patent on an isolated or purified product that has been derived from nature (including isolated DNA molecules) so long as it is distinct in "name, characteristic, and use" and it complies with the other patentability requirements. This distinction is critical, as all patentable things are products of nature in the sense that nature provides the basic source materials. *Merck & Co. v. Olin Mathieson*

Chem. Corp., 253 F.2d 156, 161-62 (4th Cir. 1958). The touchstone for patent eligibility flows from the differences in character between the isolated and native product, such differences being the product of human intervention. *See Chakrabarty*, 447 U.S. at 313 ("the relevant distinction [is] between products of nature . . . and human-made inventions"); *see also In re Bergy*, 596 F.2d 952, 976 (CCPA 1979) (recognizing that "a biologically pure culture produced by great labor in a laboratory and so claimed" is patent-eligible). Because the claimed isolated DNA molecules are distinct from their native counterparts and the result of human ingenuity, they are patent eligible.

III. The Court of Appeals' Decision Accords With The Settled Expectations Of Patent Owners.

Given the numerous risks associated with research and development, innovators must be able to rely on stable and consistent application of patent laws. *Bilski*, 130 S. Ct. at 3231 (Stevens, J., concurring) ("In the area of patents, it is especially important that the law remain stable and clear."); *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 739 (2002) (citing *Warner Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17 (1997) and reiterating that "courts must be cautious before adopting changes that disrupt the settled expectations of the inventing community").

For decades, it has been accepted that compositions isolated from nature or purified beyond their natural state are patent-eligible. *See, e.g., In re Bergy*, 596 F.2d 952; *In re Kratz*, 592 F.2d 1169

(CCPA 1979); *In re Bergstrom*, 427 F.2d 1394 (CCPA 1970); *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911). The case law addressing important biotechnology inventions developed out of chemical patent case law.[3] There is no reason in principle why isolated DNA molecules and related applications should be treated differently from other human-made polymers or small molecules.

Indeed, the USPTO Utility Guidelines state this expressly: "Like other chemical compounds, DNA molecules are eligible for patents when isolated from their natural state and purified or when synthesized in a laboratory from chemical starting materials." USPTO Utility Guidelines, 66 Fed. Reg. 1093 (2001); *see also Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc.*, 541 F.3d 1115, 1124 (Fed. Cir. 2008) (endorsing USPTO Written Description Guidelines as persuasive authority). In reliance on the settled principle that patent eligibility of isolated DNA molecules is no different than other chemical compounds, the USPTO has issued more than 50,000 patents directed to purified or isolated DNA, RNA, or amino acid sequences. *See* Subhashini Chandrasekharan & Robert Cook-Deegan, *Gene Patents and Personalized Medicine–What Lies Ahead?*, GENOME MED. 92 (2009).

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[3] *See, e.g.*, *Parke-Davis*, 189 F. at 95 (patentability of purified adrenaline extract); *Scripps Clinic and Res. Found. v. Genentech, Inc.*, 666 F. Supp. 1379 (N.D. Cal. 1987) (purified Factor VIII:C, a blood-clotting factor, patent-eligible under § 101); *In re Bergstrom*, 427 F.2d at 1394 (USPTO § 101 rejection of claims to substantially pure prostaglandin reversed).

Moreover, as this Court has recognized, § 101 is a threshold inquiry. *Bilski*, 130 S. Ct. at 3225. Assessing patent eligibility under § 101 is a prerequisite to considering the other legal requirements of patentability. *Parker v. Flook*, 437 U.S. 584, 593 (1978) ("The obligation to determine what type of discovery is sought to be patented must *precede* the determination of whether that discovery is, in fact, new or obvious.") (Emphasis added). Any claim failing the requirements of 35 U.S.C. § 101 must be rejected even if it meets all of the other legal requirements of patentability. *See In re Comiskey*, 499 F.3d 1365, 1371 (Fed. Cir. 2007) ("Only if the requirements of § 101 are satisfied is the inventor 'allowed to pass through to' the other requirements for patentability.").

For decades, courts have operated under this broad statutory framework, implicitly confirming the patent eligibility of isolated DNA sequences by addressing issues of novelty, obviousness, enablement, and written description with respect to countless patents claiming purified or isolated biological substances (including isolated DNA molecules)—issues these courts would not have reached if the inventions did not constitute patentable subject matter. [4] These cases, which

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[4] *See, e.g., In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009); *Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052 (Fed. Cir. 2005); *In re Wallach*, 378 F.3d 1330 (Fed. Cir. 2004) (claiming isolated DNA molecules encoding TNF binding proteins); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991) (claiming purified and isolated DNA sequence encoding (continued…)

turned on a range of non-threshold issues such as novelty and obviousness, lend support to the proposition that the threshold inquiry—patent eligibility—was satisfied. *See, e.g., SmithKline Beecham Corp. v. Apotex*, 403 F.3d 1331, 1352-55 (Fed. Cir. 2005) (holding that "a sua sponte inquiry into the patentability of the claimed subject matter is appropriate"); *In re Argoudelis*, 434 F.2d 1390, 1392 (CCPA 1970) (examining patent application to antibiotics extracted from strain of antibiotic-producing natural microorganism under 35 U.S.C. § 112).

Recognizing the substantial property rights involved, this Court should "be cautious before adopting changes that disrupt the settled expectations of the inventing community." *Festo Corp.*, 535 U.S. at 739 (citing *Warner Jenkinson*, 520 U.S. at 28).

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human erythropoietin); *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988); *In re Kratz*, 592 F.2d 1169 (CCPA 1979) (claiming substantially purified compound naturally-occurring in strawberries); *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958) (claiming purified vitamin B_{12}); *Kuehmsted v. Farbenfabriken of Elberfield Co.*, 179 F. 701 (7th Cir. 1910) (claims to isolated, purified salicyclic acid); *Bergstrom*, 427 F.2d at 1394 (claiming purified prostaglandins); *Parke-Davis*, 189 F. at 95 (claiming isolated adrenaline).

IV. Without Strong Patent Protection, Innovation in the Area of Biotechnology Will Decline.

The U.S. patent system is based on the notion that *some* preemption of the claimed invention leads to greater progress for society by providing an incentive to would-be inventors to share their discoveries in exchange for a limited period of exclusivity. The reward of a patent grant is the right to exclude others. 35 U.S.C. § 154(a)(1) ("Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States"). In *Mayo*, this Court acknowledged that patents by their very nature are preemptive:

> Patent protection is, after all, a two-edged sword. On the one hand, the promise of exclusive rights provides monetary incentives that lead to creation, invention, and discovery. On the other hand, that very exclusivity can impede the flow of information that might permit, indeed, spur invention, by, for example, raising the price of using the patented ideas once created.

Mayo Collaborative Servs. v. Prometheus Labs., Inc., 566 U.S. __ , 132 S. Ct. 1289, 1305 (2012).

Congress has struck a carefully-crafted bargain, encouraging innovation and public disclosure in exchange for the exclusive rights conferred by a patent. *Bonito Boats, Inc., v. Thunder*

Craft Boats, Inc., 489 U.S. 141, 146 (1989). The strength of the U.S. patent system is essential to providing appropriate incentives for continued innovation, particularly in the area of biotechnology.

Over the past several decades, Congress has witnessed the USPTO grant thousands of patents claiming isolated DNA sequences. Even while this case was pending, Congress passed the Leahy-Smith America Invents Act. This Act reformed other important aspects of the patent system, but maintained the status quo with respect to the patent eligibility question presented here. *J.E.M. Ag Supply* is instructive on this point. In that case, this Court rejected the argument that plants did not fall within the scope of § 101. 534 U.S. 124, 144-45 (2001). In doing so, this Court relied in part on the fact that "the PTO has assigned utility patents for plants for at least 16 years, and there has been no indication from either Congress or agencies with expertise that such coverage is inconsistent with [federal law]." *Id.* at 144-45. As this Court has recognized, policy concerns regarding patent eligibility are best addressed by Congress, not the courts.

A. Patent Coverage Is Vital to Protect Investment in Research.

Drug and biologics development is one of the most research-intensive industries in the world. Innovators must search for the proverbial needle in the haystack. Creating a new medicine takes, on average, an investment of ten to fifteen years and

over $1.2 billion.[5] Only two of ten marketed medicines return revenues that match or exceed the average costs of research and development. J.A. Vernon et al., *Drug Development Costs When Financial Risk Is Measured Using the Fama-French Three-Factor Model*, 19 HEALTH ECON. LETTERS 1002-1010 (2010). Patent protection provides innovators with limited exclusivity as an inducement to incur these enormous up-front costs and risks. Research, investment, and patent filing decisions must be made years in advance of marketing an FDA-approved product and as such, innovators in the field of biotechnology depend on a degree of certainty and predictability in patent law.

Patent protection of purified and isolated DNA compositions *increases* access to genetic diagnostic tests because the exclusivity conveyed in a patent grant provides the needed incentive to create the diagnostic tests in the first place. Without patent protection, the companies with the necessary expertise to develop those tests would lack incentive to undertake the enormous costs and risk associated with developing these breakthrough tests. This is especially so when contemplating the next generation of genetic diagnostic testing. Not only will it be more complex and costly to create than the

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[5] J. A. DiMasi & H.G. Grabowski, *The Cost of Biopharmaceutical R&D: Is Biotech Different?,* 28 MANAGERIAL & DECISION ECON. 467-79, 470 (2007); J. A. DiMasi & H.G. Grabowski, *Drug Discovery and Development: Understanding the R&D Process,* INNOVATION.ORG, 1-2, Feb. 2007.

first generation, but when coupled with increased clinical demands from FDA, companies could be dissuaded from investing the time and energy necessary to bring such a product to market.[6]

Moreover, the mere fact that an invention is of great importance does not mandate its free and immediate availability to all humanity. On the contrary, highly valuable inventions historically have been granted patent protection.[7] Accordingly, patentability for a valuable biotechnology product should not be vitiated because of its perceived "expense" during a limited period of exclusivity. The benefit of public disclosure of the patented invention is immediate and long-term. In the face of the enormous risks and costs required to bring a biotechnology invention to patients, many life-saving products (that are now taken for granted) would not exist without the incentive of patent protection. Patent protection provides a limited period of exclusivity, but the therapeutic value of the claimed invention endures and is available for the benefit of future generations.

Finally, empirical evidence suggests that patenting does not limit research activity. According

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[6] *See* Christopher Holman, *Will Gene Patents Derail the Next-Generation of Genetic Technologies? A Reassessment of the Evidence Suggests Not*, 80 U. MO.-KAN. L.R. 563 (2012).

[7] *See, e.g.*, U.S. Patent No. 214,636 (Edison's light bulb); U.S. Patent No. 644,077 (to acetylsalicylic acid or "aspirin"); U.S. Patent No. 821,393 (Wright Brothers' flying machine).

to one study, only one percent of academic respondents reported a project delay of more than a month due to patents on knowledge inputs necessary for their research; none reported abandoning a research project due to the existence of patents.[8]

B. Patents Spur Further Innovation.

In addition to providing incentives to companies to invest and innovate in the biotechnology field, patents serve an additional purpose of furthering innovation. For example, patent disclosures educate the research community on important advances and spark additional advancements. This exchange is efficient, allowing the public to learn from the successes and failures of others.

Protecting isolated DNA sequences spurs further progress in the area of biotechnology. In the absence of adequate patent protection, investments in innovation are subject to the "free-rider" problem in which copyists can take advantage of the pioneering work of others, stifling competition. Patents force these would-be copyists to "design around" the claimed invention, prompting competitors to develop new and potentially superior

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[8] John P. Walsh et al., *Final Report to the National Academy of Sciences' Committee on Intellectual Property Rights in Genomic and Protein-Related Inventions: Patents, Material Transfers and Access to Research Inputs in Biomedical Research* (Sept. 20, 2005).

products that might otherwise have gone undeveloped if the competitors could simply copy the earlier invention during the patent term. Indeed, research and development continues to find alternative solutions and methods for screening and early detection of breast cancer.[9]

Patent owners have relied on the broad statutory framework for patent eligibility established by Congress, decades of jurisprudence reinforcing this framework and recognizing isolated and purified biological materials as patent-eligible subject matter, and the USPTO's longstanding policy and practice with respect to those inventions. The claimed isolated DNA sequences are tangible, human-made chemical compositions whose structure, function, utility, and informational content differ from their native counterparts. This Court should uphold the settled expectations and substantial property rights of innovators and clarify that although genes as they exist in the human body are not patent-eligible, human-made "isolated" DNA sequences are patent-eligible.

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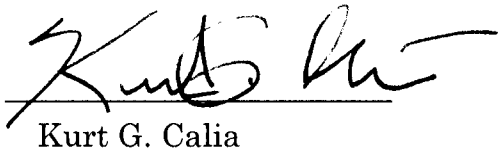
[9] *See, e.g.*, Michelle Roberts, *Way to Spot Breast Cancer Years in Advance*, BBC NEWS (May 1, 2012), http://www.bbc.co.uk/news/health-17905601.

CONCLUSION

The judgment of the court of appeals should be affirmed.

Respectfully submitted,



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