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 OF *AMICUS CURIAE* IMMATICS BIOTECHNOLOGIES, GMBH IN SUPPORT OF RESPONDENTS

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INTEREST OF *AMICUS CURIAE*[1]

Immatics Biotechnologies, GmbH ("Immatics"), is a small, for-profit corporation engaged in the business of identifying and isolating polypeptides that are useful in anti-cancer vaccines. Immatics currently has a number of vaccine compositions in clinical trials, including a renal cell carcinoma vaccine in Phase III trials, a colon cancer vaccine in Phase II trials, and numerous trials against glioblastoma in Phase I. The polypeptides forming the core of these vaccines, much like the polynucleotides at issue in this case, do not exist in nature in an isolated or purified state.

Like many small biotechnology companies, the single most valuable asset held by Immatics is its intellectual property portfolio. It is the only leverage that companies such as Immatics have to secure the continued financing necessary to extend basic research from laboratories to real-world applications. The questions of law and fact decided in this case thus will likely have a bearing on patents and patent applications owned by Immatics.

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1. No counsel representing any party to the case authored this brief in whole or in part and no counsel or party made any monetary contribution to the preparation or submission of the brief. No person other than the *amicus*, or its attorneys, made a monetary contribution intended to fund the preparation and submission of this brief. The parties have consented to the filing of this brief. Petitioners have lodged blanket consent to the filing of all amicus briefs. Respondent's consent to the filing of this amicus brief has been filed with the Clerk of Court.

SUMMARY OF THE ARGUMENT

Over at least the last 30 years, the United States Patent and Trademark Office ("USPTO") has issued thousands of patents claiming "isolated" nucleic acids, as well as other naturally-occurring chemicals claimed in isolated or purified form. Buoyed by the ability to obtain patents on such subject matter, and urged by the federal government to commercialize the results of federally-sponsored research, investigators began moving out of academic research laboratories and into private industry. As the potential for these technologies became apparent, private equity began pouring money into the industry, hoping to capitalize on the newly discovered therapeutics and diagnostic targets resulting from this research and relying on the issued patents to protect their investments.

Petitioners ask the Court to turn this well-settled order on its head by invalidating patents directed to isolated nucleic acids. According to the Petitioners, this Court's precedent excludes any subject matter containing a nucleotide sequence that exists in nature, arguing that such a patent would, in effect, claim a "product of nature." If this Court finds that "isolated" nucleic acids are unpatenable, it could call into question scores of patents covering this critical subject matter, thereby undermining the viability of these inherently risky but promising ventures.

Nothing in the Constitution, the patent statutes, or this Court's precedent justifies such a drastic action. Rather, the USPTO's practice of requiring natural products to be claimed in "isolated" form is a reasonable measure that ensures that biotechnology and pharmaceutical companies can patent this critical subject matter, without

monopolizing anything that already is "readily available to the public."

In the decision below, Judge Lourie and Judge Moore both found "isolated" nucleic acids to be patentable, but for different reasons. Judge Lourie found that isolated nucleic acids are patentable because isolation "breaks covalent bonds" relative to the longer native nucleic acid, thereby resulting in a new chemical entity. Judge Moore reasoned that, if analyzed on a blank slate, she would require the product to have a "substantial new utility" relative to its natural function in order to satisfy 35 U.S.C. § 101. While Immatics agrees that the generation of a novel chemical entity or demonstration of a new utility would be sufficient to satisfy 35 U.S.C. § 101, these are not necessary requirements.

Immatics therefore urges the Court to find that claims directed to isolated products of nature – such as the isolated nucleic acids at issue in this case – satisfy 35 U.S.C. § 101 so long as the claimed subject matter covers only compositions that (1) do not exist without human intervention and (2) have a substantial utility tied to this isolated form. The statute does not – and should not – require a change in either the chemical structure or the "essential character". This principle is consistent with the plain language of 35 U.S.C. § 101, and the cases principally relied upon by Petitioners: *Diamond v. Chakrabarty*, 447 U.S. 303, (1980), *American Fruit Growers, Inc. v. Brogdex Co.*, 283 U.S. 1 (1931), and *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948). As explained below, none of these cases requires the claimed subject matter to be directed to a novel chemical structure or a completely new activity in its isolated form.

The Petitioners characterize the test for patentability of naturally derived products as whether the inventor has transformed the "essential character" of the natural product such that it has a "distinctive name, character, or use". According to Petitioners, the isolation of a nucleic acid cannot transform it to something having a "distinctive name, character, or use" because the nucleotide sequence is its "essential character". Even assuming that this is a test for patent eligibility (which is not the case), the Petitioners have mischaracterized what subject matter satisfies this test.

The "distinctive name, character, or use" test is derived from *Hartranft v. Wiegmann*, 121 U.S. 609 (1887). In that case, the Court cites India rubber shoes as an example of subject matter that would satisfy this test, explaining that, by placing the rubber into a mold, it is transformed "into a new form capable of use and designed to be used in such new form." Therefore, contrary to the Petitioner's characterization, this test does not require a change to the "essential character" of the natural product, but that the natural product be placed into a "new form capable of use and designed to be used in such new form." An isolated nucleic acid would clearly satisfy this test, because most practical uses of the nucleic acid require it to be removed from its natural context and maintained in a substantially pure form.

This is an important point, because many new biologics and pharmaceuticals are essentially purified or synthetic versions of naturally occurring compounds. The mere fact that such compounds exist in nature does not make them readily available for human utility. Indeed, in most cases, such compounds have no practical utility in context in which they are found in nature. The process of identifying

and commercializing such products is an expensive and time-consuming proposition, often costing years of effort and hundreds of millions of dollars, with no guarantee that the candidate will ever become a viable product. For small biotechnology companies like Immatics, the only leverage that they have to ensure continued funding is the ability to patent the compounds at the core of their products.

Given that the federal government has granted such patents for at least 30 years without any action from Congress, the Court should not act to invalidate these valuable property rights.

The decision of the Court of Appeals for the Federal Circuit should therefore be affirmed.

ARGUMENT

I. The Term "Isolated" Limits the Claims to Non-Naturally Occurring Compositions Comprising the Natural Product

The USPTO has granted patents on natural products in their isolated and/or purified form for over 130 years. *See*, *e.g.*, U.S. Pat. No. 141,072, cl. 2 (filing May 9, 1873) (claiming "[y]east, free from organic germs of disease, as an article of manufacture"). This does not mean that patents issue for products as they exist in nature. By reciting that the product is isolated, the patentee is explicitly claiming the product removed from its natural context. As explained by the USPTO:

> A patent claim directed to an isolated and purified DNA molecule could cover, e.g., a gene excised from a natural chromosome or

> a synthesized DNA molecule. An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised gene is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature, or (2) synthetic DNA preparations are eligible for patents because their purified state is different from the naturally occurring compound.

66 Fed. Reg. 1092, at 1093 (Jan. 5, 2001). In addition, the form of the product that is being claimed must have a specific and substantial credible utility in the form in which it is claimed. *Id.* Thus, the USPTO's claim format limits isolated nucleic acid claims to subject matter that (1) does not exist in nature, and (2) is useful. This claim format does not require the claimed composition to possess either a novel chemical structure or a new activity relative to the product in its natural state.

Isolated compounds derived from natural sources, such as the isolated nucleic acids at issue in this case, are, by definition, man-made. Although it is often convenient to describe them in terms of chemical structure or nucleotide sequence, such "pure" or "isolated" compositions never exist in nature. Rather, they are inevitably found in complex associations with other compositions. The isolation process sometimes results in distinct chemical entities, such as the isolated nucleic acids in this case. *Ass'n for Molecular Pathology v. U.S.P.T.O.*, 689 F.3d 1303, 1328 (Fed. Cir. 2012). Other times, the result is a highly purified compound. *See, e.g.*, *Parke-Davis v. Mulford*, 189 F. 95, 103 (S.D.N.Y. 1911) (purified adrenaline); *Merck & Co. v.*

Olin Mathieson Chemical Corp., 253 F.2d 156 (4th Cir. 1958) (vitamin B12). In each case, however, the product simply does not exist in nature in an isolated form. An isolated form of such a product thus is a purely artificial, non-naturally occurring composition of matter.

II. The USPTO's Claim Format Is Consistent With the Constitution, the Patent Laws, and the Court's Precedent

The rationale for allowing such a claim is well-grounded in the Constitution, the statutes, and the case law.

A. Patenting of Isolated Products of Nature Is Consistent With the Constitutional Purpose of the Patent Laws

The Constitution does not require a claimed compound to have a formally "new" chemical structure or new function to justify a patent. Article I, Section 8 of the Constitution authorizes patents "[t]o promote the Progress of Science and useful Arts." As explained by the Court:

> Congress may not authorize the issuance of patents whose effects are to remove existent knowledge from the public domain, or to restrict free access to materials already available. Innovation, advancement, and things which add to the sum of useful knowledge are inherent requisites in a patent system which by constitutional command must 'promote the Progress of useful Arts.' This is the standard expressed in the Constitution and it may not be ignored.

Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 6 (1966). Thus, the Constitution only prohibits patents that "remove existent knowledge from the public domain" or "restrict free access to materials already available." Assuming that a claimed product satisfies 35 U.S.C. §§ 102 and 103, a patent thereto cannot "remove existent knowledge from the public domain." Likewise, the term "isolated" inherently limits the claim to subject matter that does not naturally occur. These claims therefore do not "restrict free access to materials already available." Such patents are therefore consistent with the Constitutional purpose of the patent laws.

The patent laws likewise do not prohibit patenting of isolated products of nature. Section 101 only requires that the patent claims be limited to "new" and "useful" subject matter. 35 U.S.C. § 101. This is expansive language, which "includes anything under the sun . . . made by man," and certainly any "nonnaturally occurring article of manufacture or composition of matter." *Chakrabarty*, 447 U.S. at 309 (quoting S. Rep. No. 82-1979, at 5 (1952); H.R. Rep. No. 82-1923, at 6 (1952)). As long as the claimed product does not naturally exist in isolated form, it must be considered a non-naturally occurring article of manufacture or composition of matter.

B. This Court's Precedent Only Prohibits Claims That Encompass a Natural Phenomenon as it Exists in Nature

The Court's recent ruling in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), stands for the unremarkable proposition that a patent must do more than simply claim a law of nature.

The claims at issue in *Mayo* recite a "law of nature – namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective and cause harm." *Mayo*, 132 S. Ct. at 1296. In addition to this "law of nature," the claims recite only two steps: administering a drug to a patient and observing the concentration of the metabolites in the blood. The claims of *Mayo* are thus limited only to: (1) generating the natural phenomenon by administering the drug and measuring the concentration of the metabolite (both of which were well-established in the art); and (2) observing the natural phenomenon (the correlation between concentration of the metabolite and the appropriate dosage of the drug). For this reason, the Court held that the claims do not satisfy 35 U.S.C. § 101 because the recited steps, "when viewed as a whole, add nothing significant [to the law of nature] beyond the sum of their parts taken separately" and thus effectively claim the law of nature itself. *Id.* at 1298.

This holding is along the same lines as *Bilski v. Kappos,* 130 S.Ct. 3218 (2010), *Gottschalk v. Benson*, 409 U.S. 63 (1972), and *Parker v. Flook*, 437 U.S. 584 (1978). In each of these cases, the critical issue was whether the claims cover a law of nature, natural phenomenon, or abstract idea itself, as opposed to a concrete application thereof. Such concepts are presumed to be old because they do nothing more than "reveal[] a relationship that has always existed," *Flook*, 437 U.S. at 593 n.15, and therefore "are consistent with the notion that a patentable process must be 'new and useful,'" *Bilski*, 130 S. Ct. at 3221. For process claims, 35 U.S.C. § 101 requires that "[t]he process itself, not merely the mathematical algorithm, must be new and useful." *Flook*, 437 U.S. at 591. That is,

the patent may not effectively claim subject matter that exists independent of any human intervention.

Therefore, the critical question under *Mayo* is whether the patent is limited to man-made subject matter. If so, then the subject matter is patent-eligible. If, however, the patent reads on subject matter that exists without human intervention, the claim is patent-ineligible. This concept is consistent with the USPTO's interpretation of *Chakrabarty*. As noted by the *Chakrabarty* Court, Congress intended Section 101 to broadly encompass "everything under the sun . . . made by man." *Chakrabarty*, 447 U.S. at 309 (internal citations and quotations omitted). Thus, where a claim is limited to a "non-naturally occurring article of manufacture or composition of matter," 35 U.S.C. § 101 is satisfied. *Id.* at 303.

Petitioners argue that *Funk Brothers* expands this rule to prohibit patenting of naturally-occurring products, "when [the] compositions function as they naturally would, even when human ingenuity led to their packaging in a more useful form." Pet. Br. at 29. This is not the holding of *Funk Brothers*. Each of the claims at issue in that case relates to inoculants comprising non-specific "non-inhibitive strains of . . . Bacteria." *Funk Bros.*, 333 U.S. at 128 n.1 (quoting U.S. Patent No. 2,200,532, cl. 4 (filed Aug. 24, 1938)). Thus, the patent does not claim a specific composition, but a general concept of "mutually non-inhibitive strains." As explained by Justice Frankfurter:

> [Patentee] appears to claim that since he was the originator of the idea that there might be mutually compatible strains and had practically demonstrated that some such strains exist,

> everyone else is forbidden to use a combination of strains whether they are or are not identical with the combinations that [Patentee] selected and packaged together.

Id. at 133 (Frankfurter, J., concurring). The rejected claims in *Funk Brothers* were not invalid because they claim a specific product that "functions as it naturally would." Rather, the claims were rejected because they effectively claim a natural phenomenon without an appropriate structural limitation. *See Funk Bros.*, 333 U.S. at 129-31; *cf. Mayo*, 132 S. Ct. at 1290-91. In contrast, claims to isolated nucleic acids are directed to specific products that never exist in nature in such a form. As such, neither *Funk Brothers* nor *Mayo* holds that products derived from a natural source, such as those at issue in this case, are unpatentable under 35 U.S.C. § 101.

C. Neither *Chakrabarty* nor *American Fruit Growers* requires anything beyond non-naturally occurring subject matter

Petitioners further argue that a composition is not patent eligible unless it "has a distinctive name, character and use," irrespective of whether it has a different chemical structure or character from anything existing in nature. Pet. Br. 28. According to Petitioners, isolated DNA does not have a distinctive name, character, or use or markedly different characteristics from naturally occurring DNA because the genetic sequence remains essentially the same. *Id.* at 30-31. However, neither *Chakrabarty*, *Funk Brothers*, nor *American Fruit Growers* holds that subject matter must "have a distinctive name, character, or use" or "markedly different characteristics" in order to be

"new" within the meaning of 35 U.S.C. § 101. Even if these cases did so hold, Petitioners misinterpret what is meant by these standards.

(i) The phrase "having a distinctive name, character, and use" relates solely to whether something is considered an article of manufacture

The "distinctive name, character, or use" and "markedly different characteristics" language from *Charkrabarty* and *American Fruit Growers* is not a limitation on patentable subject matter. In both cases, this language is attributed to *Hartranft v. Wiegmann*, 121 U.S. 609 (1887). *Hartranft* was not a patent case, but a customs case addressing whether a cleaned, ground, and etched shell is considered a "shell" or a "manufacture of a shell" for the purpose of calculating the appropriate customs duty. *Id.* at 612-13. The Court held that the shells at issue were not a "manufacture" because "[t]hey had not been manufactured into a new and different article, having a distinctive name, character, or use from that of a shell." *Id.* at 615.

The Court's reliance on *Hartranft* logically relates only to whether the subject matter at issue was an "article of manufacture." This question was critical in both *Chakrabarty* and *American Fruit Growers*. In *Chakrabarty*, the USPTO argued that a genetically modified living organism could not be considered an "article of manufacture." *Chakrabarty*, 447 U.S. at 310-11. Similarly, the sole issue before the *American Fruit Growers* Court was whether "an orange, the rind of which has become impregnated with borax . . . [is] a 'manufacture,'

or manufactured article." *Amer. Fruit Growers*, 283 U.S. at 11. Neither *Chakrabarty* nor *American Fruit Growers* requires all products to have a "distinctive name, character, and use" or "markedly different characteristics" in order to satisfy 35 U.S.C. § 101. Rather, demonstrating that the product has a "distinctive name, character, and use" or "markedly different characteristics" is sufficient precisely because it shows that the subject matter is an "article of manufacture."

(ii) Even if a claimed product must have a "distinctive name, character, and use" or "markedly different characteristics," this standard does not require a transformation of the "essential character" of the claimed product

Even if *Chakrabarty* and *American Fruit Growers* could be read to limit Section 101 to products "having a distinctive name, character, and use," Petitioners misconstrue what is meant by this language. According to Petitioners, isolated nucleic acids are not "new" because they contain a nucleotide sequence that naturally occurs in nature, thus retaining the same "essential character" as the naturally occurring composition. *See Ass'n for Molecular Pathology v. U.S.P.T.O.*, 689 F.3d 1303, 1355 (Fed. Cir. 2012) (Bryson, J., concurring in part and dissenting in part); Pet. Br. at 35. Thus, Petitioners argue, whether the product is different in form from its naturally occurring counterpart is irrelevant unless there is a transformation of its "essential character." *See* Pet. Br. at 35. This argument is not supported by the Court's precedent.

Hartranft again is instructive. The Court distinguished the shells in that case from another case involving India rubber shoes, noting that:

> it was held that India rubber shoes, made . . . by simply allowing the sap of the [I]ndia rubber tree to harden upon a mould, were a manufactured article, because it was capable of use in that shape as a shoe, and had been put into a new form capable of use and designed to be used in such new form.

Hartranft, 121 U.S. at 615 (citing *Lawrence v. Allen*, 48 U.S. 785 (1849)). The shoes at issue in *Lawrence* are nothing more than hardened India rubber sap. The human intervention does not change the "essential character" of India rubber sap as a raw material; it merely hardens as it would in nature. Nonetheless, human intervention, by placing the sap in a mold to harden, creates a product "having a distinctive name, character, and use" by transforming the raw material "into a new form capable of use and designed to be used in such new form." *Id.* The "transformation" did not change the "essential character" of the India rubber, but harnessed that "essential character," using human ingenuity, to craft it into a form suitable for use.

Taq polymerase provides another example. Taq is naturally produced by *Thermus aquaticus*, a bacterium found in hot springs. James H. Davis & Michele M. Wales, *The Effect of Intellectual Property on the Biotechnology Industry*, 50 Advances in Genetics 427, 437 (2003). Because it is derived from an organism that lives in high temperatures, Taq is heat stable and does not lose activity

when subjected to high temperatures. *See* Smithsonian Institution Archives, The History of PCR, RU 9577, http://siarchives.si.edu/research/videohistory_catalog9577.html (last accessed March 12, 2013).

The inclusion of Taq into a process called polymerase chain reaction ("PCR") is often cited as the single most important technological advance to the modern biotechnology industry, an achievement for which the inventors received the Nobel Prize in Chemistry. In the original iterations of PCR, new polymerase enzyme had to be added to the reaction mixture after each heat cycle, because the high temperature permanently deactivated the enzyme. *Id.* Because of its stability, Taq only needs to be added to a PCR reaction mixture once, thus greatly reducing the costs and the time of performing the process, and permitting easy automation. *Id.*

There is no principled reason why Taq should be excluded from patent eligibility. The identification and characterization of this enzyme is a significant technological advance, from which the public obtains a substantial benefit. Yet the properties of Taq that make it so attractive for PCR are a consequence of its structure and function in the natural world. In nature, just like in PCR, Taq functions as a thermostable enzyme that catalyzes the amplification of a nucleic acid. Nonetheless, assuming that 35 U.S.C. §§ 102 and 103 are satisfied, a claim to isolated Taq cannot "remove existent knowledge from the public domain." *Graham*, 383 U.S. at 6. Moreover, because Taq only exists in nature within a bacterium at a low concentration, isolated Taq is not a "material [] already available" to the public. *Id.* The only way that Taq has a practical utility is by isolating it from its natural

source. Like the India rubber example, "transformation" of Taq to an isolated form does not change the "essential character" of enzyme itself, but instead harnesses that "essential character," using human ingenuity, to craft it into a form suitable for use in PCR.

The same is true of isolated nucleic acids. Like Taq and the India rubber in *Lawrence*, naturally occurring nucleotide sequences require human intervention to transform them into something useful. By removing nucleic acids from their natural context and placing them into an isolated form, they become available for uses that are otherwise unavailable, such as:

- molecular probes for identifying related nucleic acids, *see* U.S. Patent No. 5,310,651 (filed Sept. 9, 1991);

- a gene replacement therapeutic, *see* U.S. Patent No. 6,262,035 (filed Oct. 1, 1998); and

- transforming cells into cellular "factories" for producing a variety of end products, *see* U.S. Patent No. 5,866,382 (filed Nov. 3, 1994).

Human ingenuity thus is required to place a naturally occurring nucleotide sequence into a "new form capable of use and designed to be used in such new form" by placing it in an isolated composition. *Hartranft*, 121 U.S. at 615. Consistent with *Chakrabarty*'s and *American Fruit Growers*' reliance on *Hartranft*, isolation of a nucleic acid results in a product "having a distinctive name, character, and use" from anything that occurs in nature.

(iii) The dissent's analogy to "snapping a leaf from a tree" and "newly discovered minerals" does not work

In his dissenting opinion, Judge Bryson argued that isolating a nucleic acid does not result in a "new" product, analogizing it to the act of removing a branch or a leaf from a tree or extracting a mineral from the earth. *Ass'n for Molecular Pathology*, 689 F.3d at 1350 and 1353 (Bryson, J., concurring-in-part and dissenting-in-part). However, "isolated" leaves already exist in nature without human intervention, as they often become separated from trees through natural forces, such as strong gusts of wind. Nor is human intervention required to generate a newly discovered mineral. Thus, the human intervention of removing a leaf from a tree or a mineral from the earth does not result in a new form of that leaf or that mineral. However, were one to process that leaf or mineral into a form that did not previously exist (such as a purified extract from the leaf or highly purified form of the mineral), and a patent claim were limited to that non-natural form, that transformation would result in a "new form capable of use and designed to be used in such new form." *Hartranft*, 121 U.S. at 615.

Contrary to the dissent's analogy, pharmaceuticals and biologics cannot simply be picked off of a tree or dug up from the earth. For example, the chemical entity paclitaxel (Taxol®) is naturally produced in the bark of the Pacific yew tree, *Taxus breviolia*. Jordan Goodman & Vivien Walsh, *The Story of Taxol, Nature and Politics in the Pursuit an Anti-Cancer Drug* (2001). Paclitaxel has proven to be very useful for treatment of various cancers. However, at the time that paclitaxel was identified, there was no

indication that the yew tree had any practical use, much less that it harbored anti-cancer compounds. *See id.* at 51-52. Paclitaxel is very difficult to obtain from the yew tree: 1,200 kg of bark yields only 1 kg of pure product. *Id.* at 81. The simple fact is that, without being isolated, the chemical entity paclitaxel has no practical utility at all.

The question therefore should be: does the claimed subject matter as a whole exist independent of human intervention? In *Mayo*, *Bilski*, *Flook*, *Benson*, and *Funk Brothers*, the answer was "no" because in each case the patent effectively claimed an underlying abstract idea or natural correlation. *See Mayo*, 132 S. Ct. at 1298, *Bilski*, 130 S. Ct. at 3221; *Flook*, 437 U.S. at 585; *Benson*, 409 U.S. at 64, *Funk Bros.*, 333 U.S. at 133 (Frankfurter, J., concurring). In *Chakrabarty*, the answer was "yes" because the claimed organism does not exist independent of human intervention. *Chakrabarty*, 447 U.S. at 303. Isolated nucleic acids, like the invention in *Chakrabarty*, are claimed in a form that absolutely requires the intervention of humans in order to exist. Branches, leaves, and minerals do not.

In view of the foregoing, there simply is no categorical rule that prohibits patenting of natural products in isolated form. Indeed, the clear language of 35 U.S.C. § 101 only requires that claimed "invention or discovery" be: (1) new; (2) useful; and (3) a process, article of manufacture, or composition of matter, or an improvement thereof. 35 U.S.C. § 101. Nor does the Court's precedent prohibit claims to subject matter limited solely to non-naturally occurring articles of manufacture or compositions of matter. Consistent with *Mayo* and *Funk Brothers*, such products are patentable as long as they do not claim a natural phenomenon per se. Thus, as held by *Chakrabarty*,

a non-naturally occurring composition derived from a natural source, such as the isolated nucleic acids at issue in this case, should be considered "new" within the meaning of 35 U.S.C. § 101.

III. Patents Covering Isolated Biological Products Are Critical to the Financial Viability of Biotechnology Companies and Are Deserving of Patent Eligibility

A. New biologics and pharmaceuticals are expensive to identify and difficult to bring to market, but relatively cheap and easy to copy

New pharmaceuticals and biologics do not simply grow on trees, ready to be picked like leaves, branches, and fruits, but instead require extensive research and development and costly trial and error. Researchers often screen thousands of candidates before identifying even a single compound, only to have a low probability of ever making it to market. Discovery of new biologics is even more difficult. Compared to pharmaceutical companies, the typical biotechnology company is smaller and more R&D-focused, has few internal revenue streams, and often relies solely on debt and private equity for funding. *See generally* Joseph A. Golec & John A. Vernon, *Financial Risk in the Biotechnology Industry*, Nat'l Bureau of Econ. Research, Working Paper No. 13604 (2007), http://www.nber.org/papers/w13604. As a result, "biotechnology firms face greater financial risk, and their R&D portfolios [are] even more sensitive to exposure to political and regulatory risk." *Id.* at 13.

The costs of developing new drugs and biologics is therefore staggering, averaging in excess of $400 million per approved drug as of 2002. John V. Duca & Mine K.

Yücel, *An Overview of Science and Cents: Exploring the Economics of Biotechnology,* 1 Fed. Res. Bank of Dallas Econ. & Fin. Pol'y Rev., no. 3, 2002, 4-5, *available at* http://www.dallasfed.org/assets/documents/research/efpr/v01_n03_a01.pdf. In contrast, the costs of imitation in these industries is low:

> The economics of developing new drugs differs from that of developing generic versions of existing drugs. First, the out-of-pocket costs of developing a generic are only $1 million to $2 million, far below the $400 million for developing a new drug. Second, the clinical success rate for generics is 90 to 100 percent, four to five times that of new drugs. Finally, it takes only one to two years to develop a generic versus ten to twelve years for a new drug.

Id. Patents covering naturally occurring compounds, such as the isolated nucleic acids at issue in this case, are an important part of this equation. Of 1010 new chemical entities approved for use by the Food & Drug Administration between 1981 and 2006, 399 are either biologics, natural products, or derived from natural products. David Newman & Gordon Cragg, *Natural Products as Sources of New Drugs Over the Last 25 Years*, 70 J. Nat. Prods. 461,463, tbl. 1 (2007). For biotechnology firms, these patents "are often the most crucial asset they own in a sector that is extremely research-intensive and with low imitation costs." Esteban Burrone, *Patents at the Core: the Biotech Business*, World Intellectual Prop. Org. (2006) (*available at* http://www.wipo.int/sme/en/documents/patents_biotech.htm).

Some amici have suggested that patents on isolated or purified products of nature prevent or deter future research. The opposite is true. Given the high "innovation costs" and low "imitation costs", there is little market incentive to be an innovator, because others can enter the market at a fraction of the cost and time. Strong patent protections therefore are critical to spur innovation:

> Mansfield (1986) sampled 100 firms in 12 U.S. manufacturing industries regarding their views of whether patents are important in making their decisions about investment in innovation. His results suggested that only in the pharmaceutical and chemical industries were patents considered essential, in the sense that more than 30 percent of their inventions would not have been developed in the absence of potential protection. In these sectors, fixed costs of R&D are high and imitation is fairly easy.

Keith E. Maskus, *Intellectual Property Rights in the Global Economy* 43 (Inst. for Int'l Econ 2000). Therefore, biotechnology and pharmaceutical companies must be able to obtain strong patent portfolios to justify their investment and risk. The USPTO's policy of granting patents on "isolated" products of nature fills this need without withdrawing subject matter that is already in the public commons.

B. Biotechnology companies are highly sensitive to changes in regulatory policy, including patent policy

The Solicitor now appears to be reversing policy, arguing in favor of a "Magic Microscope" test which would effectively remove all but "cDNA" type nucleic acid claims from patent-eligible subject matter.

This sudden change in policy threatens the viability of many biotechnology companies. Biotechnology companies are highly dependent on their patent portfolios for survival:

> Unlike companies in many other industries, biotechnology companies do not gain competitive advantages based on their ability to manufacture a product more quickly, easily, or cheaply than their competitors. Instead, biotechnology companies exert a competitive advantage by virtue of exclusive intellectual property rights granted to them by the United States and foreign governments for their discoveries. The key intellectual property right relied on by biotech companies is the utility patent, which grants its owner the right to exclude others from practicing its patented invention for a limited period of time. Owing to their reliance on patents, biotechnology companies have a greater sensitivity to changes and developments in patent law than do many other industries.

James H. Davis & Michele M. Wales, *The Effect of Intellectual Property on the Biotechnology Industry*, 50

ADVANCES IN GENETICS 427, 428 (2003). Additionally, the biotechnology industry is highly sensitive to regulatory events:

> Given the biotechnology industry's rapidly expanding role and contribution to the discovery and development of new drugs and biologics, it is important for policy makers to be cognizant of the fact that this industry, as a result of its dependence on external capital and the heightened sensitivity it has to policy shocks and new regulations, is more fragile with respect to its R&D projects and programs than the more established pharmaceutical industry. This is particular true for smallest biotechnology companies.

Golec & Vernon, *Financial Risk in the Biotechnology Industry*, Nat'l Bureau of Econ. Research, Working Paper No. 13604 (2007). Simply put, many biotechnology companies will not survive if the Court were to decide that isolated products of nature are not patent-eligible.

The Solicitor's reversal of policy – which was not joined by the USPTO – should be looked at with a skeptical eye. Patent-eligibility of isolated nucleic acids has been the status quo for at least the last 30 years. For over a decade, the official policy of the executive branch has been that claims limited to "isolated" or "purified" products of nature satisfy 35 U.S.C. § 101. *See generally* 66 Fed. Reg. 1092 (Jan. 5, 2001). Congress is well aware of this practice, having required the USPTO to "conduct a study on effective ways to provide independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests

exist." Leahy-Smith America Invents Act, Pub. L. No. 112–29, § 27, 125 Stat. 283, 338 (2011) (emphasis added). Despite amending the statute to explicitly exclude inventions directed to human organisms, Congress has not amended the statute to exclude isolated nucleic acids from patentability. *Id.* at § 33, 125 Stat. at 340. Any deference afforded to the Solicitor's opinion in this case is therefore undermined by decades of inaction by the executive and legislative branches.

The Court therefore should consider the damage that will be caused to the biotechnology industry before upsetting the settled expectations of the patenting community. *Festo Corp. v. Shoketsu Kinzoku Kagyo Kabushki Co.*, 535 U.S. 722, 739 (2002); *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 32 n.6 (1997).

CONCLUSION

For the reasons stated above, Immatics respectfully requests that the Court affirm the judgment of the Federal Circuit.

Respectfully submitted,

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