No. _____

IN THE

# Supreme Court of the United States

CHROMADEX, INC. AND TRUSTEES OF DARTMOUTH COLLEGE,

*Petitioners,*

v.

ELYSIUM HEALTH, INC.,

*Respondent.*

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

## PETITION FOR A WRIT OF CERTIORARI

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## QUESTION PRESENTED

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012), and *Alice Corp. v. CLS Bank International*, 573 U.S. 208 (2014), this Court established a two-step "framework for distinguishing patents that claim laws of nature, *natural phenomena*, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice*, 573 U.S. at 217 (emphasis added). Consistent with that authority, the Federal Circuit had until recently applied the *Alice/Mayo* framework to evaluate the eligibility of patents allegedly directed to any of the three patent-ineligible concepts, including natural phenomena. *See Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019). But the panel below broke with that precedent and created a split within the Federal Circuit. It saw no need to apply *Alice/Mayo* in the natural phenomena context, and instead applied a different standard derived from *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013), which omits consideration of whether a patent involves an "inventive concept."

The question presented is:

Whether the two-step *Alice/Mayo* framework governs the eligibility of patents allegedly directed to natural phenomena.

## PARTIES TO THE PROCEEDING BELOW

Petitioners ChromaDex, Inc. and Trustees of Dartmouth College were appellants in the Federal Circuit.

Respondent Elysium Health, Inc. was an appellee in the Federal Circuit.

## CORPORATE DISCLOSURE STATEMENT

Petitioner ChromaDex, Inc. is a wholly owned subsidiary of ChromaDex Corporation. Petitioner Trustees of Dartmouth College has no parent corporation, and no publicly held corporation owns 10% or more of its stock.

## TABLE OF CONTENTS

**Page**

QUESTION PRESENTED ..... i
PARTIES TO THE PROCEEDING BELOW ..... ii
CORPORATE DISCLOSURE STATEMENT ..... iii
TABLE OF AUTHORITIES ..... vi
OPINIONS BELOW ..... 1
JURISDICTION ..... 1
STATUTORY PROVISION INVOLVED ..... 1
INTRODUCTION ..... 2
STATEMENT OF THE CASE ..... 4
A. Legal Background ..... 4
B. Facts and Procedural History ..... 7
REASONS FOR GRANTING THE PETITION ..... 11
I. The Decision Below Created a Split by Determining that Patents Involving Natural Phenomena Are Exempt from the Two-Step *Alice/Mayo* Framework ..... 11
II. Dispensing with the *Alice/Mayo* Test for Claims Involving Natural Phenomena Would Frustrate Development of New Biotechnologies. ..... 17
A. The Panel's Approach Eliminates the Second, "Inventive Concept" Step of the *Alice/Mayo* Test. ..... 18

B. The Biotechnology Sector Depends on the Ability to Patent Innovative *Applications* of Natural Phenomena. .....20

III. This Case Is an Excellent Vehicle to Clarify a Discrete, Recurring Question in a Confused Area of Patent Law. .....24

CONCLUSION .....29

APPENDIX A: Court of Appeals Decision (Feb. 13, 2023) .....1a

APPENDIX B: District of Delaware Decision on Motion for Summary Judgment (Sept. 21, 2021) .....13a

APPENDIX C: Court of Appeals Order Denying Panel Rehearing and Rehearing En Banc (May 10, 2023) .....28a

## TABLE OF AUTHORITIES

**Page(s)**

**Cases**

*Aatrix Software, Inc. v. Green Shades Software, Inc.*,
890 F.3d 1354 (Fed. Cir. 2018) ..... 23, 24

*Alice Corp. v. CLS Bank Int'l*,
573 U.S. 208 (2014) ..... 2, 3, 6, 7, 11, 12, 13, 14, 16, 19, 27

*Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*,
977 F.3d 1379 (Fed. Cir. 2020) ..... 25

*Ariosa Diagnostics, Inc. v. Sequenom, Inc.*,
788 F.3d 1371 (Fed. Cir. 2015) ..... 24

*Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*,
569 U.S. 576 (2013) ..... 3, 7, 10, 13, 18

*Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*,
915 F.3d 743 (Fed. Cir. 2019) ..... 24, 25

*Berkheimer v. HP Inc.*,
890 F.3d 1369 (Fed. Cir. 2018) ..... 25

*Bilski v. Kappos*,
561 U.S. 593 (2010) ..... 5, 11

*Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*,
489 U.S. 141 (1989) ..... 4

*In re BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig.*,
774 F.3d 755 (Fed. Cir. 2014) ..... 13, 14

*Diamond v. Chakrabarty*,
447 U.S. 303 (1980) ..... 5, 7, 10, 18

*Diamond v. Diehr*,
450 U.S. 175 (1981) ..... 5

*Funk Bros. Seed Co. v. Kalo Inoculant Co.*,
333 U.S. 127 (1948) ..... 5, 18, 20, 28

*Gottschalk v. Benson*,
409 U.S. 63 (1972) ..... 6, 20, 28

*Le Roy v. Tatham*,
55 U.S. (14 How.) 156 (1852) ..... 11

*Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*,
566 U.S. 66 (2012) ..... 5, 6, 7, 12, 16, 19, 27

*Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*,
918 F.3d 1338 (Fed. Cir. 2019) ..... 3, 14, 16, 20, 27

*Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.*,
887 F.3d 1117 (Fed. Cir. 2018) ..... 19

**Statutes**

35 U.S.C. § 101 ..... 1, 5

35 U.S.C. § 102 ..... 5

35 U.S.C. § 103 ..... 5

35 U.S.C. § 112 ..... 5

**Constitutional Provision**

U.S. Const. art. I, § 8, cl. 8 ..... 4, 5

**Legislative Materials**

*The State of Patent Eligibility in America, Part I: Hearing Before the Subcomm. on Intellectual Property of the S. Comm. on the Judiciary*, 116th Cong. (June 4, 2019) (testimony of David J. Kappos, Former Director, U.S. Patent & Trademark Office) ..... 26

*The State of Patent Eligibility in America, Part II: Hearing Before the Subcomm. on Intellectual Property of the S. Comm. on the Judiciary*, 116th Cong. (June 5, 2019) (testimony of Barbara Fiacco, President-Elect of the American Intellectual Property Law Association) ..... 21

**Regulatory Materials**

*2019 Revised Patent Subject Matter Eligibility Guidance*, 84 Fed. Reg. 50 (Jan. 7, 2019) ..... 25

**Other Authorities**

Brief for Biotechnology Innovation Organization as Amicus Curiae, *Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, No. 18-1295 (Fed. Cir. Apr. 20, 2018) ..... 22

Evaluate Pharma, *World Preview 2023: Pharma's Age of Uncertainty* (Aug. 14, 2023) ..... 23

Letter from Daniel J. Staudt, President, Intellectual Property Owners Ass'n, to Andrew Hirshfeld, Interim Director, U.S. Patent & Trademark Office, re: Comments on Patent Eligibility Jurisprudence Study (Oct. 15, 2021) ..... 21, 23

Petition for Writ of Certiorari, *Am. Axle & Mfg., Inc., v. Neapco Holdings, LLC*, No. 20-891 (U.S. Dec. 28, 2020) ..... 26

Petition for Writ of Certiorari, *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, No. 19-430 (U.S. Oct. 1, 2019) ..... 26

Ryan Davis, *Courts Can Resolve Patent Eligibility Problems, Iancu Says*, Law360 (Apr. 11, 2019) ..... 26

U.S. Patent No. 2,378,876 ..... 21

U.S. Patent No. 2,449,866 ..... 21

U.S. Patent No. 2,799,620 ..... 22

U.S. Patent No. 2,908,611 ..... 21

U.S. Patent No. 3,929,992 ..... 22

U.S. Patent No. 4,894,366 ..... 22

U.S. Patent No. 4,977,138 ..... 22

U.S. Patent No. 6,190,897 ..... 22

U.S. Patent No. 7,413,887 ..... 22

U.S. Patent No. 8,383,086 ..... 9

## PETITION FOR A WRIT OF CERTIORARI

ChromaDex, Inc. and Trustees of Dartmouth College (collectively, "Petitioners") respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

## OPINIONS BELOW

The decision of the District Court is reported at 561 F. Supp. 3d 460 (D. Del. 2021), and reprinted at App. 13a–27a.

The decision of the Court of Appeals is reported at 59 F.4th 1280 (Fed. Cir. 2023), and reprinted at App. 1a–12a. The Court of Appeals' order denying panel rehearing and rehearing en banc is unreported and reprinted at App. 28a–29a.

## JURISDICTION

The Federal Circuit entered judgment on February 13, 2023, and denied Petitioners' timely rehearing petition on May 10, 2023. On August 1, Chief Justice Roberts extended the time within which to file a petition for a writ of certiorari to and including September 7, 2023. Petitioners invoke the jurisdiction of this Court under 28 U.S.C. § 1254(1).

## STATUTORY PROVISION INVOLVED

Title 35, Section 101 of the U.S. Code provides: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof,

may obtain a patent therefor, subject to the conditions and requirements of this title."

## INTRODUCTION

Petitioners seek review of a Federal Circuit decision that conflicts with this Court's reigning patent-eligibility framework, creates an intracircuit split, and threatens to chill innovation across the biotechnology sector.

This case arises from the invention of a dietary supplement containing nicotinamide riboside ("NR"), a vitamin that increases the production of nicotinamide adenine dinucleotide ("NAD+"), a coenzyme that improves human health—for example by strengthening the body's defenses against various diseases. NR is found naturally in milk, but in that form, it does not increase NAD+ production and thus does not produce human health benefits. It is only by *isolating* NR and *formulating* it for administration that it becomes useful. The patent at issue thus claims a "composition" that includes NR, is "formulated for oral administration," *and* "increases NAD+ biosynthesis upon oral administration."

If the panel below had properly applied this Court's operative *Alice/Mayo* framework, it would have had no trouble concluding that this inventive application of a naturally occurring substance was patent eligible under 35 U.S.C. § 101. The *Alice/Mayo* framework is used to "distinguis[h] patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible *applications* of those concepts." *Alice Corp. v. CLS Bank Int'l*, 573 U.S. 208, 217 (2014)

(emphasis added). The test asks, first, whether a patent is "directed to" a patent-ineligible topic; and second, whether the patent nevertheless reflects an "inventive concept" that *applies* that subject matter in a novel or useful manner. Because the patent at issue here claims a new and useful *application* of NR—by isolating it and formulating it for oral administration—it satisfies Section 101 under *Alice/Mayo*.

But the Federal Circuit panel applied a different test, derived from *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013). The panel determined that the claims were not patent eligible after concluding that the isolated NR composition claimed by the patent does not have "markedly different characteristics" compared to naturally occurring NR. The panel stated that its "inquiry could end" there because the *Alice/Mayo* framework does not apply to claims "directed to a natural phenomenon." That ruling not only contradicted this Court's instruction that the *Alice/Mayo* framework applies to "natural phenomena," *Alice*, 573 U.S. at 217, it also split with *Natural Alternatives Int'l, Inc. v. Creative Compounds, LLC*, 918 F.3d 1338 (Fed. Cir. 2019), which applied the *Alice/Mayo* framework in the natural phenomena context and upheld a similarly structured patent involving beta-alanine, a naturally occurring substance.

The panel's decision threatens far-reaching consequences for the biotechnology sector. If the one-step *Myriad* standard displaces the two-step *Alice/Mayo* framework, there will be no "inventive

concept" inquiry for claims that implicate natural phenomena. That approach would erase this Court's longstanding recognition that novel *uses* and *applications* of a patent-ineligible concept are nevertheless patentable. Because entire biotechnological industries depend on the ability to develop—and protect through patent rights—novel *uses* and *applications* of naturally occurring substances, the harms to innovation in the biotechnology sector would be particularly severe.

This Court should grant review, resolve the Federal Circuit split that the panel has created, and confirm that *Alice/Mayo* applies with equal force in the context of natural phenomena.

## STATEMENT OF THE CASE

### A. Legal Background

1. Recognizing the importance of innovation to the Nation's future, the U.S. Constitution empowers Congress "[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." U.S. Const. art. I, § 8, cl. 8. Since 1790, Congress has exercised this authority through repeated iterations of the federal Patent Act. 35 U.S.C. §§ 101, *et seq.*; *see also Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146–48 (1989) (detailing history of statutory patent protection).

The Patent Act broadly provides that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or

any new and useful improvement thereof, may obtain a patent therefor . . . ." 35 U.S.C. § 101. Section 101 is "cast in broad terms to fulfill the constitutional and statutory goal of promoting 'the Progress of Science and the useful Arts' with all that means for the social and economic benefits." *Diamond v. Chakrabarty*, 447 U.S. 303, 315 (1980) (quoting U.S. Const. art. I, § 8, cl. 8.)

Section 101 must also be interpreted in light of its role as one of many statutory requirements for patent validity. To obtain a patent, an inventor must meet Section 101's threshold requirement of an inventive concept and "also satisfy" additional statutory requirements, "includ[ing] that the invention be novel, nonobvious, and fully and particularly described." *Bilski v. Kappos*, 561 U.S. 593, 602 (2010) (citing 35 U.S.C. §§ 102–103, 112 (2006)).

This Court has limited the broad terms of eligibility in Section 101 by establishing judicially created exceptions for "laws of nature, natural phenomena, and abstract ideas." *Diamond v. Diehr*, 450 U.S. 175, 185 (1981). The Court recognized these three implied limitations on the theory that the material they cover should be "free to all men and reserved exclusively to none." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

At the same time, this Court has warned that "too broad an interpretation of this exclusionary principle could eviscerate patent law." *Mayo Collaborative Servs. v. Prometheus Lab'ys, Inc.*, 566 U.S. 66, 71 (2012). Because "all inventions embody, use, reflect, rest upon, or apply laws of nature, natural

phenomena, or abstract ideas" to an extent, "[a]pplications of such concepts to a new and useful end . . . remain eligible for patent protection." *Alice*, 573 U.S. at 217 (2014) (cleaned up) (quoting *Mayo*, 566 U.S. at 71; *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). Courts accordingly must "tread carefully in construing this exclusionary principle lest it swallow all of patent law." *Id.*

2. More recently, in a pair of decisions—*Mayo* (2012) and *Alice* (2014)—this Court has formalized a two-step test for analyzing patent eligibility under Section 101. The Court has described this approach as "a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice*, 573 U.S. at 217.

At *Alice/Mayo* step one, a court asks "whether the claims at issue are directed to one of those patent-ineligible concepts"—*i.e.*, to "laws of nature, natural phenomena, and abstract ideas." *Id.* If the claims are *not* directed to such a concept, that is the end of the Section 101 inquiry, and the claims are eligible for patent protection.

At *Alice/Mayo* step two, a court searches for an "'inventive concept'—*i.e.*, an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Id.* at 217–18 (quoting *Mayo*, 566 U.S. at 72–73). The court "consider[s] the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements

'transform the nature of the claim' into a patent-eligible application." *Id.* at 217 (quoting *Mayo*, 566 U.S. at 78–79).

Despite instructing that the *Alice/Mayo* framework applies in the "natural phenomena" context, *Alice*, 573 U.S. at 217, this Court did not apply that framework in *Myriad*, which addressed the patent eligibility of claims directed to certain DNA segments and was decided after *Mayo* but before *Alice*, *see* 569 U.S. at 582–83. Rather than apply *Alice/Mayo*, the Court evaluated whether the claim was directed to a product "with markedly different characteristics from any found in nature." *Id.* at 590–91 (quoting *Chakrabarty*, 447 U.S. at 310). The Court determined that the naturally occurring DNA segments were not patent eligible under that standard, but that synthetic DNA sequences were patent eligible because their creation resulted in molecules that were "distinct from the DNA from which [they were] derived." *Id.* at 591–95.

After deciding *Myriad*, this Court reaffirmed in *Alice* that Section 101 calls for a two-step "framework for distinguishing patents that claim laws of nature, *natural phenomena*, and abstract ideas from those that claim patent-eligible applications of those concepts." 573 U.S. at 217 (emphasis added).

### B. Facts and Procedural History

1. The invention here relates to isolated nicotinamide riboside (known as "NR"), a unique form of vitamin B3 for use in oral dietary supplements. Isolated NR facilitates production of nicotinamide adenine dinucleotide ("NAD+"), a coenzyme vital to

cellular function and associated with numerous biological activities. App. 14a. NAD+ levels decrease with age, Fed. Cir. J.A. 2918, and also as a result of physiological stresses, such as those that result from alcohol consumption, excess nutrients, or sun exposure, Complaint at 6 (Dist. Ct. Dkt. 1). Stimulating NAD+ production is often beneficial because NAD+ deficiencies can cause diseases in both animals and humans. *See* App. 2a. Isolated NR formulated for oral administration enhances NAD+ biosynthesis safely and more effectively than other known forms. Fed. Cir. J.A. 10192. Un-isolated NR occurs naturally in cow's milk, but naturally occurring NR has no impact on NAD+ levels, Fed. Cir. J.A. 10166, and so does not generate the positive health effects of isolated NR, Fed. Cir. J.A. 10162–10163. In other words, it is only by isolating, purifying, and concentrating NR that it becomes beneficial to health. *See* Fed. Cir. J.A. 10174–10175, 10180.

The invention is claimed by U.S. Patent No. 8,197,807 ("the '807 Patent"). Among other things, the '807 Patent claims:

> 1. A composition comprising isolated nicotinamide riboside in combination with one or more of tryptophan, nicotinic acid, or nicotinamide, wherein said combination is in admixture with a carrier comprising a sugar, starch, cellulose, [or other enumerated substance], wherein said composition is formulated for oral administration and increases NAD+ biosynthesis upon oral administration.

App. 3a.

The named inventor, Dr. Charles Brenner, is a former professor of genetics and biochemistry at the Dartmouth Medical School, one of four professional and graduate schools in Dartmouth College, a nonprofit educational research institution. Dartmouth is the assignee of the '807 Patent. Fed. Cir. J.A. 2510.

In 2012, Dartmouth granted ChromaDex an exclusive license to make, use, and/or sell products and processes covered by the '807 Patent. App. 3a; Fed. Cir. J.A. 1498. ChromaDex is a global nutraceutical company that sells, among other products, dietary supplements under the brand name TRU NIAGEN®. These products are pharmaceutical compositions of isolated NR that embody the invention claimed in the '807 Patent. App. 3a.

2. Elysium formerly purchased ChromaDex's isolated NR product for use in its own BASIS® supplement products. After those purchases ceased, Dartmouth and ChromaDex filed suit alleging that Elysium's manufacture and sale of its BASIS® products infringe various claims of the '807 Patent. App. 3a.[1]

Following claim construction and expert discovery, Elysium moved for summary judgment, arguing that the asserted claims of the '807 Patent claim a product of nature that is ineligible for patent protection under 35 U.S.C. § 101. App. 3a–4a. In response, Petitioners

[1] Petitioners also initially alleged infringement of U.S. Patent No. 8,383,086. Those claims are not at issue here.

disputed that the asserted claims cover an unpatentable natural phenomenon and submitted unrebutted evidence regarding the inherent properties of isolated NR, which distinguish the claims from naturally occurring NR. Fed. Cir. J.A. 10100.

3. On September 21, 2021, the district court granted summary judgment to Elysium, concluding that the asserted claims of the '807 Patent claim an unpatentable natural phenomenon. App. 20a–27a.

The court of appeals affirmed. App. 2a. The court started with the conclusion that the '807 Patent "claims are very broad and read on milk," a "naturally occurring product that is not patent eligible" and includes "tryptophan . . . [that] treats NAD+ deficiencies." App. 5a–6a. Eschewing *Alice*'s two-step framework, the court compared the '807 Patent's claims to the inventions at issue in *Myriad*, 569 U.S. at 589, and *Chakrabarty*, 447 U.S. at 309. App. 7a–9a. Focusing on *Myriad*'s rationale, the court held that the '807 Patent's claims to isolated NR "do not have characteristics markedly different from milk," App. 9a, in which tryptophan "increases NAD+ biosynthesis," App. 9a–10a (acknowledging that "milk increases NAD+ biosynthesis . . . because it contains tryptophan rather than because of the trace amounts of NR"). Despite acknowledging that the claimed compositions differ from what exists in nature, the court determined that the claims are "broad enough to encompass a product of nature." App. 9a.

Stating that its "inquiry could end here," the court of appeals added a conclusory "resort to *Alice/Mayo*."

App. 11a. But that half-page analysis merely incorporated the *Myriad* discussion by reference. It rested, at step one, on "the reasons stated above," and, at step two, on the court's view that neither recognizing the benefits of isolated NR nor isolating it are sufficiently "inventive" to warrant patent eligibility. App. 11a. For those propositions, the court cited only one case: *Myriad*.

On May 10, 2023, the court of appeals denied Petitioners' petition for panel and *en banc* rehearing. App. 28a–29a.

## REASONS FOR GRANTING THE PETITION

### I. The Decision Below Created a Split by Determining that Patents Involving Natural Phenomena Are Exempt from the Two-Step *Alice/Mayo* Framework.

In *Alice*, this Court made clear that the two-step *Alice/Mayo* framework applies to patents purportedly addressed to "natural phenomena." *Alice*, 573 U.S. at 217. The panel's decision disregards that authority and splits with published Federal Circuit precedent.

A. For more than 150 years, this Court has held that "three specific" categories of subject matter—laws of nature, natural phenomena, and abstract ideas—are not patentable. *Bilski*, 561 U.S. at 601–02; *see also Le Roy v. Tatham*, 55 U.S. (14 How.) 156 (1852). And in *Mayo* and *Alice*, the Court "set forth a framework for distinguishing patents that claim laws of nature, *natural phenomena*, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice*, 573 U.S. at 217 (emphasis

added). As outlined above, *see supra* pp. 6–7, step one of the framework involves "determin[ing] whether the claims at issue are directed to one of those patent-ineligible concepts," and step two focuses on whether there is an "inventive concept" that transforms the claims into a "patent-eligible application." *Alice*, 573 U.S. at 217–18.

In *Mayo*, the Court happened to apply that two-part framework to patents that addressed "laws 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 or cause harm." 566 U.S. at 77. And in *Alice*, the Court happened to apply the same framework to claims that were drawn to the "abstract idea" of "exchanging financial obligations between two parties using a third-party intermediary to mitigate settlement risk." 573 U.S. at 219.

But in neither case did the Court suggest that the two-part framework would *not* apply to "natural phenomena"—*i.e.*, the third of the three patent-ineligible concepts. To the contrary, in both cases, the Court strongly suggested that the two-part framework applied with equal force to the "natural phenomena" category. *See, e.g.*, *Mayo*, 566 U.S. at 82 ("[S]imply appending conventional steps, specified at a high level of generality, to laws of nature, *natural phenomena*, and abstract ideas cannot make those laws, *phenomena*, and ideas patentable." (emphasis added)); *Alice*, 573 U.S. at 217 (explaining that *Mayo* "set forth a framework for distinguishing patents that claim laws of nature, *natural phenomena*, and

abstract ideas from those that claim patent-eligible applications of those concepts" (emphasis added)).

Nevertheless, in *Myriad*—which was decided after *Mayo* but before *Alice*—the Court addressed the eligibility of a patent encompassing natural phenomena *without* applying the two-step *Alice/Mayo* framework. *See* 569 U.S. at 589–90. The Court held that "a naturally occurring DNA segment" is a patent-ineligible "product of nature," but that "synthetically created DNA" (or cDNA) "is patent eligible because it is not naturally occurring" and "is distinct from the DNA from which it was derived." *Id.* at 580, 595; *see also id.* at 589–96. Rather than applying the two-step *Alice/Mayo* framework, the Court framed the question before it as "whether Myriad's patents claim any 'new and useful . . . composition of matter,' or instead claim naturally occurring phenomena." *Id.* at 590 (alteration in original) (citation omitted).

One year later, the Court reaffirmed in *Alice* that the two-step framework applies to "natural phenomena." 573 U.S. at 21.

B. The Court's conflicting signals regarding whether the *Alice/Mayo* framework applies in the context of natural phenomena have sown division in the Federal Circuit.

Initially, in *In re BRCA1- & BRCA2-Based Hereditary Cancer Test Pat. Litig.*, 774 F.3d 755, 759 (Fed. Cir. 2014), the Federal Circuit suggested that different frameworks may apply depending on the type of subject matter at issue. The court first applied *Myriad*—without the *Alice/Mayo* framework—to

address the eligibility of a composition-of-matter claim directed to "[a] pair of single-stranded DNA primers for determination of a nucleotide sequence of a BRCA1 gene." *Id.* at 759–61. The court then proceeded to apply the *Alice/Mayo* framework to evaluate the eligibility of a related method claim, explaining that the "two-step test" outlined in those cases applied whether the claim was allegedly addressed to a "law of nature" or an "abstract ide[a]." *Id.* at 761–65. That approach implied that the *Alice/Mayo* test does *not* apply to claims purportedly covering natural phenomena.

But in *Natural Alternatives*, the Federal Circuit expressly determined otherwise. It explained that the *Alice/Mayo* framework applies to assess whether a patent covers "ineligible concepts of laws of nature, *natural phenomena*, and abstract ideas." 918 F.3d at 1342 (quoting *Alice*, 573 U.S. at 216–17) (emphasis added). The Federal Circuit then applied the *Alice/Mayo* framework to determine the eligibility of various patents related to a natural product—*i.e.*, dietary supplements containing beta-alanine. *See id.* at 1342, 1347, 1349. At step one, the court held that the claims were not directed to natural phenomena because while they were "directed to specific treatment formulations that incorporate natural products," the claims "have different characteristics and can be used in a manner that beta-alanine as it appears in nature cannot." *Id.* at 1348. For good measure, the court also rejected the eligibility challenge at *Alice/Mayo* step two, since the specification did not convey that the relevant dietary supplement limitation was "well-understood, routine, and conventional." *Id.* at 1347, 1349.

*Natural Alternatives*, then, appeared to resolve the confusion: It correctly held that the *Alice/Mayo* framework applies to all three patent-ineligible categories, including natural phenomena.

3. Enter the decision below, which like *Natural Alternatives*, considered the eligibility of a patent addressed to compositions containing a natural substance that had been isolated and incorporated into a dosage form with particular health-improving characteristics. To evaluate that question, the panel invoked *Myriad* and its predecessor, *Chakrabarty*, asserting that those were the only two Supreme Court authorities that "apply here." App. 7a. The panel then focused its inquiry on a standard it derived from those cases: whether the "claimed compositions . . . exhibit markedly different characteristics from natural milk." App. 8a. The panel held that because the "claims lack markedly different characteristics from milk," they "claim a product of nature and are not patent eligible of nature." App. 11a. In other words, the panel reached its holding without applying the two-step *Alice/Mayo* framework—and indeed, before even citing *Alice* or *Mayo*.

The panel thus noted that its "inquiry could end here." *Id*. There was no need to apply the *Alice/Mayo* framework because "the Supreme Court in *Myriad* relied on *Chakrabarty*'s 'markedly different characteristics' framework for analyzing whether the claimed compositions there were directed to a natural phenomenon," and "never applied the *Alice/Mayo* two-step framework." *Id.* The panel did not acknowledge that *Alice*—which postdated *Myriad*—expressly directed that the two-step framework

should be used "for distinguishing patents that claim laws of nature, *natural phenomena*, and abstract ideas from those that claim patent-eligible applications of those concepts." 573 U.S. at 217 (emphasis added). And the panel mischaracterized *Natural Alternatives*, asserting that the opinion "functionally examined only the *Chakrabarty* question"—*i.e.*, the markedly different characteristics analysis. App. 11a n.5. As discussed, *Natural Alternatives* applied both *Alice/Mayo* prongs and addressed (among other things) whether the claimed steps were "well-understood, routine, and conventional." 918 F.3d at 1347, 1349.

After determining that the *Alice/Mayo* framework did not apply, the panel purported to apply it anyway—but in name only. The panel addressed *Alice/Mayo* step one in a half-sentence, "conclud[ing] [that] the asserted claims are directed to a product of nature *for the reasons stated above*." App. 11a (emphasis added). In other words, the panel simply incorporated its *Myriad*-based analysis by reference. Similarly, the panel addressed *Alice/Mayo* step two in a short paragraph and by citing a single authority: *Myriad*. App. 13a. The panel did not engage in an actual *Alice/Mayo* step two analysis. For example, it did not "consider the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Alice*, 573 U.S. at 217 (quoting *Mayo*, 566 U.S. at 78–79). Nor did the panel evaluate whether isolating NR was "well-understood, routine, conventional activity previously engaged in by

researchers in the field." *Mayo*, 566 U.S. at 73; *accord Alice*, 573 U.S. at 225.

Due to the panel's decision, it is once again unclear—in the Federal Circuit and therefore nationwide—what framework applies to evaluate the patent eligibility of claims involving natural phenomena. Is it *Alice/Mayo*, *Myriad*, or some combination of the two? As explained below, the answer is consequential.

## II. Dispensing with the *Alice/Mayo* Test for Claims Involving Natural Phenomena Would Frustrate Development of New Biotechnologies.

Addressing whether *Alice/Mayo* or *Myriad* governs the patent-eligibility inquiry in the natural phenomena context is not a mere labeling exercise. Because there are meaningful, substantive differences between the two standards, the stakes are high—both for the validity of patents and for the innovation that they incentivize.

Simply put, because *Myriad* is best understood as an *Alice/Mayo* step one inquiry, replacing *Alice/Mayo* with *Myriad* would effectively mean eliminating *Alice/Mayo* step two—*i.e.*, the search for the "inventive concept," through which the *use* or *application* of an otherwise patent-ineligible concept becomes patentable. Jettisoning that step would be problematic in any context. But it would cause special harms in the natural phenomena space, where entire biotechnological industries depend on the ability to develop—and protect through patent rights—novel *applications* of naturally occurring substances. These

real-world harms underscore the need for this Court's review.

### A. The Panel's Approach Eliminates the Second, "Inventive Concept" Step of the *Alice/Mayo* Test.

*Myriad* is best read as addressing step one of the *Alice/Mayo* framework: whether the claims at issue were "directed to" natural phenomena. *Myriad* asked whether the relevant patents "claim[ed] naturally occurring phenomena." 569 U.S. at 590. The Court concluded that "naturally occurring, isolated DNA segments" were not patent eligible because they were not "markedly different" from those found in nature, but that synthetic cDNA was patent eligible because it was "an exons-only molecule that is not naturally occurring." *Id.* at 590–95 (cleaned up). In other words, *Myriad* focused on the threshold question whether the patents were "directed to" natural or artificial compositions.

*Myriad* also relied on authorities that focused on step one of the *Alice/Mayo* test. In *Chakrabarty*, for example, the Court determined that an artificially modified bacterium was not a natural phenomenon but "a nonnaturally occurring manufacture or composition of matter" because it had four extra plasmids and a "capacity for degrading oil." 447 U.S. at 305, 310 & n.1. By contrast, in *Funk Brothers*, a mere mixture of naturally occurring bacteria was a natural phenomenon because the relevant bacteria had not been altered. 333 U.S. at 128–32.

Conspicuously absent from the *Myriad* family of cases is any discussion of *Alice/Mayo*'s second step:

the "search for an 'inventive concept'—*i.e.*, an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Alice*, 573 U.S. at 217–18 (quoting *Mayo*, 566 U.S. at 72–73). The "inventive concept" component of the *Alice/Mayo* analysis is critical. It clarifies that an inventive *application* of otherwise patent-ineligible subject-matter can "transform the nature of the claim" such that it survives Section 101. *Alice*, 573 U.S. at 217 (quoting *Mayo*, 566 U.S. at 78).

In *Mayo*, for example, the patent failed to satisfy the "inventive concept" inquiry because its claims "add[ed] nothing of significance to the natural laws themselves." 566 U.S. at 87. But the result would have been different if the claims had "confine[d] their reach to particular *applications* of those laws"—like "a typical patent on a new drug or a new way of *using* an existing drug." *Id.* (emphasis added); *see also Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117 (Fed. Cir. 2018) (claims were patent eligible where they "recite[d] more than the natural relationship between CYP2D6 metabolizer genotype and the risk of QTc prolongation" by "recit[ing] a method of treating patients based on this relationship").

*Natural Alternatives*—the Federal Circuit authority that properly applied *Alice/Mayo* in the context of claims similar to those here and thus conflicts with the decision below—illustrates how the "inventive concept" step should operate in the natural phenomena context. There, the court reasoned that "even if" the relevant claims at *Alice/Mayo* step one

were "directed to" ineligible natural phenomena—including the amino acid beta-alanine—they could still be eligible for patent protection at step two. *See id.* at 1347, 1349. Specifically, the patent claims required that the beta-alanine be "provided through a dietary supplement," and a fact question remained as to whether "the dietary supplement in the claims, which provides a dose well in excess of the normal levels of beta-alanine, would have been well-understood, routine, and conventional." *Id.* That is, an inventive *application* or *use* of beta-alanine—a naturally occurring amino acid—would be patent eligible.

*Myriad*'s one-step focus on whether the relevant composition is "markedly different" from any composition found in nature reserves no space for this broader analysis. *Myriad* asks whether a claimed composition *itself* is naturally occurring. But that cannot mark the end of the inquiry. After all, it is settled that the "application" of a "hitherto unknown phenomenon of nature" to a "new and useful end" is patent eligible. *Gottschalk v. Benson*, 409 U.S. 63, 68 (1972) (quoting *Funk Bros.*, 333 U.S. at 130). *Alice/Mayo*'s "inventive concept" framework implements that basic patentability principle.

### B. The Biotechnology Sector Depends on the Ability to Patent Innovative *Applications* of Natural Phenomena.

Replacing the two-step *Alice/Mayo* framework with the more limited *Myriad* inquiry would do particular harm to the biotechnology sector, which is

largely built on developing new *uses* and *applications* for naturally occurring substances.

Innovation in this area has historically been spurred by the availability of patent protection. *See* Letter from Daniel J. Staudt, President, Intellectual Property Owners Ass'n, to Andrew Hirshfeld, Interim Director, U.S. Patent & Trademark Office, re: Comments on Patent Eligibility Jurisprudence Study (Oct. 15, 2021), https://perma.cc/WJK8-SFMG. But that dynamic would be threatened if a narrow reading of *Myriad* were permitted to overtake the broader *Alice/Mayo* approach in the natural phenomena context. Present and future patents that address the inventive application of natural compositions would lack a firm foothold in this Court's patent-eligibility jurisprudence. With the validity of such patents in doubt, investments would diminish and innovation would be chilled. *See The State of Patent Eligibility in America, Part II: Hearing Before the Subcomm. on Intellectual Property of the S. Comm. on the Judiciary*, 116th Cong. (June 5, 2019) (testimony of Barbara Fiacco, President-Elect of the American Intellectual Property Law Association), at 2, https://perma.cc/V4TR-6FEG.

The industries that comprise the biotechnology sector are numerous and varied. But there is a common thread: All are focused on development of technology derived to some extent from naturally occurring substances. Patent protection has historically fostered the innovation of these technologies. Examples include:

- **Antibiotics:** Many antibacterial and antifungal medicines were first isolated from natural sources and patented. *See, e.g.*, U.S. Patent No. 2,908,611 (amphotericin b); U.S. Patent No. 2,449,866 (streptomycin); U.S. Patent No. 2,378,876 (actinomycin); U.S. Patent No. 2,799,620 (neomycin).

- **Industrial enzymes:** Phytase, an enzyme supplement to animal feed, enhances the ability of livestock to digest phytate in grain, thus reducing environmental pollution from fecal phosphate. *See, e.g.*, U.S. Patent No. 6,190,897. Glucoamylase, an enzyme from the fungus *Trichoderma reesei* that efficiently releases glucose sugars from carbohydrates, allows for better production of biofuels such as ethanol. *See, e.g.*, U.S. Patent No. 7,413,887.

- **Immunosuppressive drugs:** Drugs used to prevent organ rejection of transplant recipients were discovered in natural, soil-dwelling microbes. *See, e.g.*, U.S. Patent No. 4,894,366 (tacrolimus); U.S. Patent No. 3,929,992 (sirolimus/rapamycin).

- **Anticancer compounds:** Many cytostatic drugs were discovered, isolated, and derived from botanical or microbial sources. For instance, romidepsin is an isolate from *Chromobacterium violaceum* from a soil sample obtained in Japan, and is used to treat cutaneous T-cell lymphoma. *See* U.S. Patent No. 4,977,138.

In addition, as a leading biotechnology trade association has noted, various crop protection products and plant breeding products also implicate technologies that involve novel applications and uses of naturally occurring substances. *See* Brief for Biotechnology Innovation Organization as Amicus Curiae, *Natural Alternatives*, No. 18-1295 (Fed. Cir. Apr. 20, 2018), ECF No. 28.

These critical innovations are made possible only through sizeable private investments in research and development. In the United States alone, the biotechnology industry is responsible for more than 100 billion dollars of annual research investment.[2] And those investments are predicated on the availability of patent protection. Biotechnology businesses attract capital and commercial partners based on the expectation that those investments will generate an expected return on investment in the form of patent-protected products or services. If novel applications of naturally occurring substances are no longer patentable, the health of the biotechnology sector would be threatened. Indeed, industry experts have noted that "[i]t is impossible to quantify the cost to society if medicines cannot be developed because the current section 101 jurisprudence is too restrictive." Staudt, Comments on Patent Eligibility Jurisprudence Study, *supra*.

The need for investments in the biopharmaceutical space continues. For example, "[w]e are all aware of

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[2] *See* Evaluate Pharma, *World Preview 2023: Pharma's Age of Uncertainty* (Aug. 14, 2023), https://bit.ly/3r22ynM (reporting R&D in the pharmaceutical sector alone at $249 billion in 2021).

the need for new antibiotics because bacteria have become resistant to our existing products." *Aatrix Software, Inc. v. Green Shades Software, Inc.*, 890 F.3d 1354, 1361 (Fed. Cir. 2018) (Lourie, J., concurring in denial of petition for rehearing en banc). "Nature, including soil and plants, is a fertile possible source of new antibiotics," and "[i]ndustry should not be deprived of the incentive to develop such products that a patent creates." *Id.*

This Court should grant certiorari to clarify that the *Alice/Mayo* framework—and its recognition that inventive *applications* of naturally occurring substances may be patentable—applies with equal force in the natural phenomena context.

## III. This Case Is an Excellent Vehicle to Address a Discrete, Recurring Question in a Confused Area of Patent Law.

This petition offers an ideal opportunity to provide clarity on a narrow—but important—legal issue in a muddled area of this Court's jurisprudence.

A. The decision below is far from the first time that the Federal Circuit has misapplied this Court's patent-eligibility jurisprudence. Section 101 has been a frequent source of confusion within the Federal Circuit, often giving rise to fractured opinions. *See, e.g.*, *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, 967 F.3d 1285 (Fed. Cir. 2020), *reh'g denied*, 966 F.3d 1347 (Fed. Cir.), *cert. denied*, 142 S. Ct. 2902 (2022); *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, 915 F.3d 743 (Fed. Cir. 2019), *reh'g denied*, 927 F.3d 1333 (Fed. Cir.), *cert. denied*, 140 S. Ct. 855

(2020); *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015), *reh'g denied*, 809 F.3d 1282 (Fed. Cir.) (per curiam), *cert. denied*, 579 U.S. 928 (2016).

Indeed, the ongoing uncertainty has caused nearly "every judge on [the Federal Circuit] to request Supreme Court clarification" regarding the proper application of Section 101. *Am. Axle & Mfg., Inc. v. Neapco Holdings LLC*, 977 F.3d 1379, 1382 (Fed. Cir. 2020) (Moore, J., concurring in denial of stay). For example, Judge Hughes has noted that the "fraught [] issue of § 101 eligibility" "is not a problem that [the Federal Circuit] can solve," and has invited this Court to provide "further explication." *Athena Diagnostics*, 927 F.3d at 337 (concurring in the denial of rehearing en banc). Judge Chen has observed that the Federal Circuit is "not in a position to resolve" the "present confusion," "but the Supreme Court can." *Id.* at 1349 (Chen, J., concurring in the denial of rehearing en banc). And Judges Lourie and Newman have proclaimed that "Section 101 issues certainly require attention beyond the power of this court." *Berkheimer v. HP Inc.*, 890 F.3d 1369, 1374 (Fed. Cir. 2018) (concurring in the denial of rehearing en banc).

The United States Patent and Trademark Office has similarly requested clarification of this Court's patent-eligibility standards. The "need for more clarity and predictability" has hindered the Office's efforts to provide guidance to its more than 8,500 patent examiners and administrative patent judges. *2019 Revised Patent Subject Matter Eligibility Guidance*, 84 Fed. Reg. 50, 50 (Jan. 7, 2019). Applying patent-eligibility precedent has become "increasingly

. . . difficult" and has led to "inconsistent results"; "something needs to be done to increase clarity and consistency." *Id.* at 50, 52. Former PTO Director Andrei Iancu has declared patent eligibility "the most substantive patent law issue in the United States. And it's not even close." Ryan Davis, *Courts Can Resolve Patent Eligibility Problems, Iancu Says*, Law360 (Apr. 11, 2019), https://perma.cc/R9KV-DXK7. And Former Director David Kappos has called patent-eligibility law "truly . . . a mess," with the Patent and Trademark Office "spinning [its] wheels on decisions that are irreconcilable, incoherent, and against our national interest." *The State of Patent Eligibility in America, Part I: Hearing Before the Subcomm. on Intellectual Property of the S. Comm. on the Judiciary*, 116th Cong. (June 4, 2019) (testimony of David J. Kappos), at 1–2, https://perma.cc/XDD8-BXRD.

B. This Court has understandably declined previous invitations to reconstruct its Section 101 jurisprudence from the ground up. *See, e.g.*, Petition for Writ of Certiorari at 1, *Athena Diagnostics, Inc. v. Mayo Collaborative Servs., LLC*, No. 19-430 (U.S. Oct. 1, 2019) (urging Court to "provide much-needed guidance on the proper application of [all three] judicially-created exceptions to Section 101" and identifying "five points of confusion" in need of clarification); Petition for Writ of Certiorari at 33, *Am. Axle & Mfg., Inc., v. Neapco Holdings, LLC*, No. 20-891 (U.S. Dec. 28, 2020) (urging Court to grant review to address "both the substantive and procedural questions plaguing the lower courts").

But this petition is not like its Section 101 predecessors. Although the potential effects of the Federal Circuit's decision are broad, *see supra* section II, the question presented is narrow. It asks only whether this Court's *Alice/Mayo* framework—which indisputably applies in the context of abstract ideas and laws of nature—*also* applies to natural phenomena, the third patent-ineligible concept. The narrowness of the question is a virtue: It would allow this Court to make measured progress in clarifying its Section 101 jurisprudence without risking collateral damage to an already fragile patent-eligibility framework.

C. This case is also an excellent vehicle for addressing that question. The panel squarely determined that the Section 101 "inquiry could end" after applying *Myriad*'s "markedly different characteristics" standard because there was no need to apply "the *Alice/Mayo* two-step framework" to patents involving natural phenomena. App. 11a. By announcing that approach, the panel created an intracircuit split with *Natural Alternatives*, where the Federal Circuit dutifully applied both of the *Alice/Mayo* steps in the natural phenomena context. *See* 918 F.3d at 1342, 1347, 1349.

Further, resolving the question presented will control the outcome of this case. If the panel had actually (rather than nominally) applied the *Alice/Mayo* framework, it would have correctly determined that the '807 Patent is patent eligible under Section 101. Because the panel substituted a one-step *Myriad*-focused analysis for the two-step *Alice/Mayo* framework, the panel neglected to

undertake any substantive consideration of whether the '807 Patent reflects an "inventive concept" that renders the claims patent eligible. *See Alice*, 573 U.S. at 217–18 (quoting *Mayo*, 566 U.S. at 72–73). The panel thus never asked whether the '807 Patent contains "an element or combination of elements that is 'sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.'" *Id.*

Applying that standard, it is clear that the '807 Patent *does* contain an inventive concept that renders it patent eligible under Section 101. The patent not only addresses the therapeutic benefits of isolated NR, but also the *application* of that insight by claiming a particular composition of isolated NR that is formulated for oral administration such that it is bioavailable. NR as it naturally exists in trace amounts in milk is not bioavailable. And while the '807 Patent does not claim an altered molecular structure of NR, it does claim a novel formulation of NR that is bioavailable, and that can be orally administered as a safe and effective vehicle to improve health. That "application" of a "phenomenon of nature" to a "new and useful end" is patent eligible. *Gottschalk*, 409 U.S. at 68 (quoting *Funk Bros.*, 333 U.S. at 130).

## CONCLUSION

For the reasons set forth above, the Court should grant the petition for a writ of certiorari.

Respectfully submitted,

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