No. 18-127

In the Supreme Court of the United States

Amgen Inc., Amgen Manufacturing Limited, and Amgen USA, Inc.,

Petitioners,

v.

Sanofi, Aventisub LLC, Regeneron Pharmaceuticals Inc., and Sanofi-Aventis U.S., LLC,

Respondents.

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

BRIEF OF *AMICI CURIAE* BRISTOL-MYERS SQUIBB COMPANY, MORPHOSYS AG, BAVARIAN NORDIC A/S, AND UCB BIOPHARMA SPRL IN SUPPORT OF PETITIONERS

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TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Regulations

Other Authorities

INTEREST OF AMICI CURIAE[1]

Amici curiae are innovator biopharmaceutical companies that spend billions of dollars researching and developing cutting-edge therapies for patients with unmet medical needs. These therapies have led to treatments for myriad life-threatening conditions, including various types of cancer and autoimmune diseases. Amici rely on patents to protect their groundbreaking inventions, to ensure that they receive a reasonable return on their enormous investments in biopharmaceutical research and development, and to fund the next generation of research and development of innovative treatments.

Amici believe that the Federal Circuit's current jurisprudence on 35 U.S.C. § 112 — exemplified by the decision below — is erroneous. The Federal Circuit's approach makes it exceedingly difficult to obtain robust patent protection for biopharmaceutical innovations and consequently impedes progress in this field.

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[1] Amici and their counsel have authored the entirety of this brief, and no person other than amici or their counsel has made a monetary contribution to the preparation or submission of this brief. Counsel for amici confirms that, while they are counsel for Petitioner Amgen on other matters, they are not counsel in this proceeding. Counsel of record for Petitioners and Respondents received timely notice of amici's intention to file this brief and have consented to its filing.

INTRODUCTION AND SUMMARY OF THE ARGUMENT

This case concerns the question of what an inventor must disclose to the public to obtain a patent on a biotechnology invention, such as a therapeutic antibody.

Antibodies are proteins that precisely bind to molecular targets (called "antigens") and thereby cause a certain response in the human body — for example, interfering with the target's role in promoting disease. Antibody-based therapies have revolutionized modern medicine and have led to unprecedented success in treating various cancers, autoimmune diseases, and other conditions, many of which previously had no known treatment.[2] Because they target disease-causing mechanisms better than previous small-molecule therapies, therapeutic

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[2] *See* FDA, *What are "Biologics" Questions and Answers* (2018), https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm; Li, et al., Synergistic anti-tumor therapy by a comb-like multifunctional antibody nanoarray with exceptionally potent activity, *Nature.com* (2015), https://www.nature.com/articles/srep15712 at 1; Deborah J.L. Wong & Sara Hurvitz, Recent advances in the development of anti-HER2 antibodies and antibody-drug conjugates, *NCBI* (2014), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4260046/ (similar); David E. Gerber, *Targeted Therapies: A New Generation of Cancer Treatments*, Am. Fam. Physician, at 316 (Fed. 1, 2008), *available at* https://www.aafp.org/afp/2008/0201/p311.html.

antibodies also offer the promise of fewer and more manageable side effects.[3]

Last year, therapeutic antibodies represented five out of the top ten best-selling pharmaceutical products: Avastin® (cancer), Remicade® (rheumatoid arthritis), Herceptin® (cancer), Rituxan® (autoimmune diseases and cancer), and Humira® (autoimmune diseases).[4] Other highly effective antibodies include Opdivo® and Keytruda®, both so-called anti-PD-1 checkpoint immunotherapy antibodies that have redefined the standard of treatment for cancer patients; treatment with one anti-PD-1 antibody completely eliminated 91-year old President Jimmy Carter's metastasized cancer in 2015.[5] Another dramatic example of the importance of therapeutic antibodies involves metastatic neuroblastoma, a rare pediatric cancer of the nervous system. In the past two decades, clinicians have used therapeutic antibodies to increase the long-term survival rate for individuals with this disease from near zero to sixty percent.[6]

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[3] *See, e.g.*, Gerber, *supra*; Wong & Hurvitz, *supra*.

[4] *See* A. Philippidis, *The Top 15 Best-Selling Drugs of 2017* (Mar. 12, 2018), https://www.genengnews.com/the-lists/the-top-15-best-selling-drugs-of-2017/77901068?page=1.

[5] Cancer Research Institute, *Immunotherapy Fact of the Day # 20*, https://www.cancerresearch.org/join-the-cause/cancer-immunotherapy-month/30-facts/20.

[6] Memorial Sloan Kettering Cancer Center, *Monoclonal Antibody Drugs for Cancer Treatment* (Dec. 1, 2008),

As researchers continue to unlock the enormous potential of therapeutic antibodies, the outsized impact of these drugs on the medical landscape is likely only to grow.

The first step in developing a therapeutic antibody is to discover in the body the underlying molecular target to which the antibody binds, the connection between the target and the disease, and the pathways that the antibody may activate or inhibit. Next, the inventor must generate at least one antibody that is capable of precisely binding to the specified target; find a way to manufacture that antibody on a sufficiently large scale; and test the resulting antibody for safety and efficacy, eventually in large-scale clinical trials.

This process is complex — and expensive. The cost of bringing a biologic (the category of drugs of which antibodies are a part) to market averages $2.6 billion.[7] In the last decade, biopharmaceutical companies — like amici here — "have invested half a

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https://www.mskcc.org/blog/monoclonal-antibody-drugs-treatment.

[7] Carmela De Luca & Anastassia Trifonova (2017): Patent disclosure requirements for therapeutic antibody patents, *Expert Opinion on Therapeutic Patents*, DOI:10.1080/13543776.2017.1296950; *see also* PhRMA, *2016 profile: Biopharmaceutical Research Inudstry*, http://phrma-docs.phrma.org/sites/default/files/pdf/biopharmaceutical-industry-profile.pdf.

trillion dollars" in research and development.[8] In 2016 alone, "biopharmaceutical companies invested about $90 billion in R&D in the United States — more than any other industry in America."[9] To ensure that these companies receive a reasonable return on those investments — and thus that they are incentivized to make the investments in the first place to fund the next generation of innovative treatments — it is critical that the companies be able to obtain robust patent protection on their inventions.[10] This is especially the case for small- to medium-sized biopharmaceutical companies, which require outside funding from venture funds, banks, or large pharmaceutical partners to pursue cutting-edge research and development for complex biologics.

But obtaining robust patent protection is easier said than done. The underlying targets, connections, and pathways may be considered natural phenomena, which cannot be easily patented under this Court's cases interpreting 35 U.S.C. § 101. *See, e.g.*, *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012). It is therefore crucial that innovators be able to obtain patent protection on the antibodies themselves. But once the underlying target and pathways to disease

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[8] PhRMA, *2018 Profile: Biopharmaceutical Research Industry*, *https://www.phrma.org/industryprofile/2018/*.

[9] *Id.*

[10] *See* De Luca & Trifonova, *supra*, at 1.

have been discovered, and an antibody capable of precisely binding to that target has been generated, it may be routine and conventional — and not necessarily innovative — to manufacture similar antibodies that also precisely bind to that target and treat the same disease. These follow-on antibodies may differ from the original antibody with respect to the underlying protein (amino-acid) sequence, though each follow-on antibody retains (i) the properties of being an antibody, (ii) the ability to bind to the target, and (iii) the same therapeutic properties.

Thus, a patent limited to a *single* antibody (i.e., an antibody defined by its specific protein sequence) may not protect against copycat products. The patentee, having invested enormous sums in discovering the underlying target and its mechanism to treat disease, has simply provided a blueprint for free-riders who, now aware of the target, can quickly make their own antibodies that avoid the narrow patent.[11] To ensure these breakthrough discoveries are adequately rewarded, the patentee must be able to obtain protection on an entire *group* (or "genus") of antibodies that bind to the desired target.

The question presented here is what the patentee must disclose in the patent specification to

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[11] *See, e.g.*, Rush to protect lucrative antibody patents kicks into gear, *Nature* (May 25, 2018), https://www.nature.com/articles/d41586-018-05273-z [hereinafter "*Nature*"].

adequately describe such a group of antibodies. 35 U.S.C. § 112 requires that a specification "contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art … to make and use" the invention. The Federal Circuit has interpreted § 112 to contain two separate requirements: an "enablement" requirement (that the specification enable a person of skill to make and use the invention) and a "written description" requirement (that the specification show "possession" of the invention). *See* Pet. App. 16a; *see generally Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

As Amgen explains in its petition for certiorari, the Federal Circuit has repeatedly acted contrary to the statute and to this Court's case law by cleaving the unitary standard of § 112(a) into two separate requirements — "enablement" and "written description." This Court should grant review to correct that mistake and ensure that § 112 is applied the way Congress wrote it.

The Federal Circuit's reimagining of the statutory standard is particularly problematic in the context of inventions like the one at issue here, which is drawn to a genus of therapeutic antibodies. The Federal Circuit has interpreted its extra-statutory "possession" standard to require that the inventor disclose a "representative number of examples" of the genus. That rigid requirement is an exceedingly poor fit in the context of biotechnology

inventions, and makes patents of a scope commensurate with the inventors' contributions to the field very difficult to obtain. It is reminiscent of other inflexible standards that have been adopted by the Federal Circuit and rejected by this Court: for example, the "machine or transformation" test for patent eligibility, rejected as unduly rigid in *Bilski v. Kappos*, 561 U.S. 593 (2010), and the "teaching, suggestion, or motivation" test for obviousness, rejected as unduly rigid in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007). The Court should likewise reject the Federal Circuit's misreading of the statute and its rigid test here and instruct that court to analyze § 112(a) in a flexible, contextual way, with attention to all applicable factors supported by the statute. The number of examples disclosed in the specification may be "a useful and important clue, an investigative tool, for determining whether" the patentee has adequately described her invention — but it "is not the sole test." *Bilski*, 561 U.S. at 604.

This Court should grant certiorari.[12]

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[12] Amici take no position on whether Amgen's patent claims in this case satisfy § 112(a); amici maintain that the Federal Circuit evaluated the claims under the wrong standard. This Court should grant certiorari, reverse, and remand with instructions to evaluate the Amgen claims under a more flexible test.

ARGUMENT

I. THE FEDERAL CIRCUIT ERRED BY INTERPRETING § 112(a) TO CONTAIN A FREESTANDING "WRITTEN DESCRIPTION" REQUIREMENT THAT THE INVENTOR SHOW "POSSESSION" OF THE INVENTION

Our nation's patent laws reflect a fundamental *quid pro quo*. An inventor discloses her invention to the public, thereby adding it to the collective body of knowledge. In return, the inventor gets a patent: the right to exclude others from making, using, or selling the invention for a limited period of time. *See Universal Oil Prods. Co. v. Globe Oil & Refining Co.*, 322 U.S. 471, 484 (1944).

The first pillar of this *quid pro quo* — the disclosure requirement — is enshrined in 35 U.S.C. § 112(a), which provides that a patent specification "shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains . . . to make and use the same." If the inventor makes the requisite disclosure, she receives the "reward" of a patent monopoly. *Universal Oil*, 322 U.S. at 484.

Section 112(a) requires a written description of the invention and of the manner of making and using it. This is a unitary requirement: whether the description enables a skilled artisan to make and use

the invention. *See, e.g.*, Pet. 17. This unitary interpretation both accords with the plain language of the statute and reflects the purpose of the disclosure requirement: ensuring that future innovation may build on the work reflected in patent disclosures. *See Evans v. Eaton*, 20 U.S. (7 Wheat) 356, 433–34 (1822). The Federal Circuit's interpretation of § 112(a) to include a freestanding requirement that the patentee show "possession" of the invention, in contrast, is divorced from the statute's language and fails to serve the statute's purpose.

This Court's precedents reinforce the plain-meaning reading of § 112(a). In *The Telephone Cases*, for example, the Court held that Alexander Graham Bell's claim to a method of transmitting speech telegraphically was valid because he had "described, with sufficient precision to enable one of ordinary skill in such matters to make [the invention]." 126 U.S. 1, 535 (1888). The Court recognized that Bell had not yet built a telephone that transmitted words well enough "so that they could be distinctly heard and understood." *Id.* "[It] is enough," the Court explained, that a patentee *"describes his method with sufficient clearness and precision to enable those skilled in the matter* to understand what the process is, and if he points out some practicable way of putting it into operation." *Id.* at 536 (emphasis added). In other words, Bell's patent's disclosure was still sufficient because it met the statute's *enablement* requirement. *The Telephone Cases* thus undermines the Federal

Circuit's holding that the law imposes a written-description requirement separate from enablement.

Similarly, in *Markman v. Westview Instruments, Inc.*, the Court explained that a patent specification must "describ[e] the invention in such full, clear, concise, and exact terms *as to enable any person skilled in the art to make and use the same*." 517 U.S. 370, 373 (1996) (emphasis added); *accord Mayo*, 566 U.S. at 90. This language further buttresses the conclusion that the sole standard found in § 112(a) is "a written description . . . to enable"; there is no separate "possession" standard.

The Federal Circuit's decision in *Ariad Pharmaceuticals* relied principally on two cases from this Court — *Evans v. Eaton* and *Schriber-Schroth Co. v. Cleveland Trust Co.*, 305 U.S. 47 (1938) — to conclude that § 112(a) contains a written-description requirement separate from enablement. Neither of those cases, however, supports the Federal Circuit's analysis.

The *Evans* Court stated that a patent specification "has two objects": (i) "to make known the manner of constructing the [invention] so as to enable arti[s]ans to make and use it" and (ii) "to put the public in possession of what the party claims as his own invention, so as to ascertain if he claim [*sic*] any thing that is in common use, or is already known." 20 U.S. at 433–34. But this language merely reflects the state of the Patent Act when *Evans* was decided: back then, patents had no claims, and so the statute explicitly required that

the specification contain a "written description of [the] invention, and of the manner of using . . . in such full, clear and exact terms, as [i] to distinguish the same from all other things before known, and [ii] to enable any person skilled in the art . . . to make . . and use the same." Patent Act of 1793, 1 Stat. 318, § 3. The requirement that the specification distinguish the invention from the prior art was removed when Congress amended the statute to require claims. *See, e.g.*, 35 U.S.C § 112(b). Today, the *claims* serve the function of distinguishing the invention from the prior art, and the specification need only enable one of skill in the art to make and use the claimed invention. Thus, *Evans* cuts *against* the idea that § 112(a) contains anything other than a basic description that enables the invention.

Schriber-Schroth does not support the Federal Circuit's position either. As two dissenting judges in *Ariad* recognized, *Schriber-Schroth* was about *priority*: whether the patent applicant's original specification properly disclosed the subject matter that the applicant later wished to include in amended claims. *See* 305 U.S. at 57–58. *Schriber-Schroth* thus "stand[s] only for the unremarkable proposition that an applicant cannot add new matter to an original disclosure." *Ariad*, 598 F.3d at 1363 (Rader, J., dissenting).

In sum, this Court has consistently assessed the disclosure required by § 112(a) according to a unitary standard: the description must enable a skilled artisan to make and use the invention. The Court has *never* held that the statute also contains a

separate "written description" requirement under which the patentee must show "possession" of the invention by including a "representative number of examples," and nothing in the statutory text supports the Federal Circuit's decision to create one. The Federal Circuit's approach is contrary to law and has negative policy implications: as Amgen explains in its petition, that court's application of the amorphous "possession" standard has been unpredictable and destabilizing, and it threatens to impede the development of groundbreaking technologies, particularly in the biotechnology space. Pet. 17–33. Review is warranted so that this Court may correct the Federal Circuit's erroneous course.

II. THE UNWARRANTED EXTENSION OF THE "POSSESSION" STANDARD BEYOND ITS HISTORICAL ROOTS IS ERRONEOUS AND IMPERILS INNOVATION IN THE BIOPHARMACEUTICAL INDUSTRY

A. "Possession" Of An Invention Was A Concept Originally Developed In The Context Of Claim Support And Priority, Not As A Freestanding Requirement Apart From Enablement

From the enactment of the modern Patent Act in 1952 until the Federal Circuit's 1997 decision in *Regents v. Eli Lilly*, the concept of "possession" was used to evaluate whether an applicant had a written description in the specification that was adequate to

support the claims and demonstrate priority. The patent examiner or a court might review a claim that was amended during patent prosecution to consider whether the amended claim had support in the specification. Or, the court or examiner might consider if the applicant or patentee had described a claimed invention at her earliest priority date, so as to (a) "swear behind" alleged prior art, 37 C.F.R. § 1.131; (b) demonstrate the date of invention of an embodiment encompassed by an interference count in order to win a priority contest, *see, e.g.*, *Coleman v. Dines*, 754 F.2d 353, 359 (Fed. Cir. 1985); or (c) add or amend a claim in an application years after filing by showing that the added or amended material was indeed in a priority document, *see, e.g.*, *In re Rasmussen*, 650 F.2d 1212, 1214 (C.C.P.A. 1981). "Possession" in that context was understandable and easy to apply: Was the invention described at the date of priority? *See Ariad*, 598 F.3d at 1363–64 (Rader, J., dissenting); *see also Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003) (patent application must "recount [the inventor's] invention in such detail that his future claims can be determined to be encompassed within his original creation").

In 1997, with its decision in *Regents v. Eli Lilly*, 119 F.3d 1559 (Fed. Cir. 1997) the Federal Circuit suddenly expanded the "possession" test beyond the narrow context of support for claim language and made it a freestanding requirement of the specification under § 112 — thereby cleaving the

unitary standard of the statute in two. 119 F.3d at 1566. The Federal Circuit ratified its freestanding "possession" standard *en banc* in the 2010 *Ariad* decision and then subsequently created rigid sub-tests to implement it.

As discussed in the following sections, the Federal Circuit's wrong turn has had serious consequences, especially vis-à-vis claims to groups of biological molecules such as antibodies. The court's current written-description jurisprudence, if allowed to stand, will severely prejudice innovators in the biopharmaceutical field, in ways Congress never intended in enacting § 112.

B. After The Decision Below, An Inventor Can Claim A Group Of Antibodies Only If She Satisfies The Federal Circuit's Rigid "Representative Number of Examples" Sub-Test

In an effort to make sense of its expanded extra-statutory "possession" standard, the Federal Circuit initially created at least three separate sub-tests for determining whether a patentee had adequately described a genus of biological molecules, such as antibodies: (i) the "common structural features" sub-test, (ii) the "fully characterized antigen" sub-test, and (iii) the "representative number of examples" sub-test. *See, e.g.*, Pet. App. 12a–13a (noting the district court's instruction to the jury that written description could be shown by reference to any of these three tests). As the Federal

Circuit's "possession" jurisprudence has evolved, however, these sub-tests have progressively narrowed, to the point that the "representative number of examples" sub-test is now effectively the only one left.

In the antibody-genus context, the "common structural features" sub-test (i) — which requires the patentee to "disclos[e] structural features common to the members of the genus," Pet. App. 14a — is virtually impossible to satisfy in light of the sequence diversity of antibodies.[13] A group of antibodies, all of which have the same antibody-molecule structure and same functional effect of precisely binding to a common antigen/target, may have markedly disparate protein sequences, and it is usually not possible for the inventor to define a common structure in all that sequence diversity in a way that adequately captures the genus.

Under the "fully characterized antigen" sub-test (ii), if a patentee discloses a fully characterized antigen, "either by its structure, formula, chemical name, or physical properties, or by depositing a protein in a public depository, the [patentee] can then claim an antibody by its binding affinity to that described antigen." *Noelle v. Lederman*, 355 F.3d 1343, 1349 n.4 (Fed. Cir. 2004). That is because, since "antibody technology is well developed and mature," it may be routine and conventional for skilled artisans to generate similar antibodies that

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[13] *See Nature*, *supra*.

bind to an antigen once the antigen itself is fully characterized. *Id.*

This sub-test at least had the virtue of being consistent with the purpose of § 112: ensuring that the patentee discloses the manner of making and using the invention in exchange for patent exclusivity. Describing a fully characterized antigen generally enables a person of skill in the art to make and use a similar antibody corresponding to the invention. *See, e.g.*, Elvin A. Kabat, Structural Concepts in Immunology and Immunochemistry 46 (2d ed. 1976). The "fully characterized antigen" sub-test thus provided reasonable patent protection for pioneers in the field of therapeutic antibodies — patent protection commensurate with the inventors' contributions to the field. In the decision below, however, the Federal Circuit — after close to fifteen years of use — jettisoned this test altogether, concluding that "[t]he test was not central to the holding in . . . *Noelle*." Pet. App. 16a.

The upshot is that, under current Federal Circuit law, a patentee wishing to adequately describe a group of antibodies *must* satisfy the "representative number of examples" sub-test (iii) for possession; there are no other avenues. As explained in the following section, however, the Federal Circuit is applying even that sub-test in an increasingly stringent manner, thereby making patent protection harder and harder to obtain in this field — and reducing incentives for innovation as a result.

C. The Federal Circuit Has Applied The "Representative Number Of Examples" Sub-Test In An Increasingly Strict — And Erroneous — Manner

The Federal Circuit's departure from the language of § 112 and its current application of the "representative number of examples" sub-test for possession have created significant practical problems for patentees in recent years.

First, the "representative number of examples" sub-test requires a patentee who claims a group of antibodies to describe, in great detail, the protein sequences of an *indeterminate* number of antibodies that fall within the group. For example, in *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, the Federal Circuit found a claim to a genus of antibodies invalid for lack of written description, even though the patentee had "describe[d] the amino acid sequence of about 300 antibodies" having the required functional characteristics. 759 F.3d 1285, 1291, 1300 (Fed. Cir. 2014). The court found that all 300 were encompassed within "one type of structurally similar antibody" that was "not representative of the full variety or scope of the genus." *Id.* However, in any given case, it is generally impossible for a patentee to know in advance whether she has described a sufficiently large — and sufficiently "representative" — number, so as to meet the Federal Circuit's test.

Second, the test ignores the basic fact that, while "antibodies are structurally complex, . . . many changes to their amino-acid sequences *will not affect their function*." *Nature*, *supra* (emphasis added). The Federal Circuit requires that the patentee disclose a "representative" sample without consideration of whether the differences among the various antibodies in the genus are material to the antibody's *binding function* and its ability to treat disease. *See* Pet. App. 19a. The "representativeness" inquiry is thus divorced from the fundamental nature of the invention — i.e., the invention of a group of antibodies with a precise binding function.

Third, because it is impossible to predict the protein sequence of an antibody before an antibody is made (in contrast to determining an antibody's ability to bind to a target, which can be determined using well-known and conventional technology), the "representative number of examples" sub-test implicitly but necessarily requires that the patentee actually reduce to practice — that is, actually make — multiple antibodies in the genus prior to filing a patent application. *See Abbvie Deutschland*, 759 F.3d at 1300; *see also* Pet App. 19a–20a. This runs afoul of the Federal Circuit's own case law, which unequivocally holds that actual reductions to practice are *not* required to satisfy the written-description requirement. *See Falkner v. Inglis*, 448 F.3d 1357, 1366–67 (Fed. Cir. 2006).

Fourth, and perhaps most troublingly, the Federal Circuit has permitted patent challengers to use *after-arising embodiments* — antibodies created

after the patent application was filed — to show that the patentee did not describe a representative number of examples of the genus at the filing date. *See* Pet. App. 7a–12a. This means that a patentee, having adequately described what she justifiably believed was a representative number of examples of the claimed genus at the time of filing, may later find that her once-valid patent has suddenly become *invalid* because of the post-filing discovery of other, previously unforeseen (and perhaps unforeseeable) examples. In other words, a patentee can now never be sure that an infringer will not be able to use the patentee's own disclosure to create, years after the filing date, undescribed examples that fall within the genus claim, and then invalidate the claim for not having described these after-arising antibodies.

Indeed, this is precisely what happened in *Abbvie Deutschland*. The Federal Circuit held an antibody-genus claim invalid for lack of written description because, post-filing, the accused infringer had made antibodies that (i) clearly infringed and (ii) functioned as the antibodies described and claimed by the patentee, yet (iii) had structural differences unrelated to the antibody's ability to function. 759 F.3d at 1300. And the same thing could happen in this case: the twenty-plus examples of antibodies described in Amgen's patents may later turn out not to be "representative" of the claimed genus if, on remand, Sanofi is allowed to introduce evidence of additional antibodies it may have made after the priority date of the patents — even as recently as yesterday.

D. The Decision Below Will Hinder Innovation In The Biopharmaceutical Industry And Impede The Development Of Innovative Therapies For Patients In Need

The Federal Circuit has made it far too difficult for pioneers of therapeutic antibodies to obtain sufficiently robust and reliable patent protection for their inventions. By insisting on one narrow and inflexible sub-test, the court has divorced the statutory inquiry from the true nature of innovation in this field. Innovators who discover and disclose new targets and pathways and a method of producing corresponding antibodies should receive, in exchange, the reward of sufficient patent protection. That is the fundamental *quid pro quo* of our patent laws. The Federal Circuit's approach has saddled these inventors with a virtually impossible task: reducing to practice and describing a number of members of the genus that is sufficiently large and diverse that the court will be sure to deem it "representative."

What is more, even if a patentee can generate a "representative number" of examples as of the filing date (through rote preparation and sequencing of additional antibodies after the original innovative antibody is invented), the patentee has no way of knowing if a challenger will later be able to create other antibodies that render the described ones no longer representative. And in any event, such an exercise, carried out solely for patent purposes,

diverts resources from supporting further innovation. Indeed, for small biopharmaceutical companies and universities, the implicit requirement for an indeterminately large number of pre-filing actual reductions to practice may preclude these entities entirely from obtaining patent protection on their discoveries, since they lack the resources to carry out such a task.[14] And for larger biopharmaceutical companies, the requirement diverts valuable resources away from efforts to discover the next breakthrough innovations, and toward efforts to generate repetitive, non-innovative actual reductions to practice. In effect, the Federal Circuit's test gets the incentives exactly backwards: it encourages incremental advances, rather than fundamental ones.

The Federal Circuit's approach puts patent protection in the United States at a distinct disadvantage vis-à-vis other patent jurisdictions where more flexible rules are applied. For example, the European Patent Office does not require a patentee claiming a genus of antibodies "to provide evidence that an antibody has actually been produced if the target is susceptible to routine methods of antibody production."[15] The Canadian Intellectual Property Office applies a similar rule:

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[14] *See Nature*, *supra*.

[15] News from Abroad: Antibodies in the European Patent Office, *Patent Docs* (2016); *see also* JA Kemp, Antibody Prosecution in the European Patent Office (Feb. 2013).

"claims to an antibody specific for a novel antigen can be obtained even in the absence of working examples if the antigen is sufficiently described."[16] That is essentially the (now abandoned) holding of *Noelle*. The lack of broad U.S. patent protection for a group of antibodies relative to other jurisdictions threatens to decrease investment in pioneering biotechnology research in the United States.

III. THE FEDERAL CIRCUIT SHOULD TREAT § 112(a) IN A UNITARY FASHION AND ANALYZE THE STATUTE IN A FLEXIBLE, MULTI-PRONGED, CONTEXTUAL MANNER

The key component missing from the Federal Circuit's present approach to § 112(a) — especially as applied to biotechnology inventions — is *flexibility*. A one-size-fits-all test will not work; as the *Noelle* court recognized, "each case involving the issue of written description[] 'must be decided on its own facts.'" 355 F.3d at 1349 (citation omitted). Consider the following example: As described above, it may be conventional and routine to generate additional similar antibodies (with immaterial structural differences) that precisely bind to a fully characterized antigen once a single such antibody has been invented. However, discovery of a *specific* antibody that binds to the antigen and has superior functional properties may well require that the patentee fully disclose the structure of the specific

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[16] De Luca & Trifonova, *supra*, at 2.

antibody, such as by providing its amino acid sequences.

In short, every case is different, and a flexible, adaptable standard is required — not a rigid, unvarying rule like the "representative number of examples" sub-test now applied by the Federal Circuit to its putatively separate written-description inquiry. Just as in *Bilski* and *KSR*, the Federal Circuit has created a narrow and inflexible rule where, instead, a multi-pronged, contextual inquiry is needed. And just as in those cases, this Court's review is warranted to correct the Federal Circuit's mistake.

The Federal Circuit has previously analyzed § 112 in a holistic, flexible, context-specific manner, in both the "written description" and "enablement" contexts. In *Capon v. Eshhar*, for example, the court, recognizing that "[t]he 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge," articulated a multi-factor inquiry. 418 F.3d 1349, 1358–59 (Fed. Cir. 2005). The court indicated that the nature of the invention, breadth of the claims, the state of the technology, level of skill in the art, and predictability are relevant factors for both the written description and enablement factors, effectively collapsing both inquiries into a single test supported by the statute. No one factor was dispositive under the *Capon* test; the weight to be accorded each factor depends on the circumstances of the particular case. *See id.*

The multi-factor *Capon* test largely tracks the test the Federal Circuit applies in the (at present, separate) enablement context, *see In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The "*Wands* factors" include the majority of the *Capon* factors, and add the amount of experimentation and the presence of working examples in the specification. The "presence of working examples" factor in *Wands* essentially foretells by about a decade the "representative number of examples" sub-test from *Regents* and *Ariad*.

In comparing the *Capon* and *Wands* factors, Judge Linn has pointed out the obvious: the *Capon* factors for written description "mirror the *Wands* factors for enablement." *Ariad*, 598 F.3d at 1368 (Linn, J., dissenting). It is hardly surprising that the factors for written description and enablement are "mirrors" of each other; both inquiries have their genesis in 35 U.S.C. § 112. Written description and enablement are but twin components of the same statute and should be analyzed in a unitary fashion.

The standard of § 112, whether called "enablement," "written description," or something else, should be applied as it was in *Capon* and *Wands*: in a context-specific manner, with attention to all relevant considerations in each particular case. In the context of antibody-based therapies, the standard should reintegrate *Noelle*'s "fully characterized antigen" sub-test as one possible route for the patentee to show that she has provided an adequate written description of the invention, so as to enable it. The standard could even incorporate

the "representative number of examples" sub-test. Indeed, in *Wands*, the presence or absence of "working examples" is one of eight factors to evaluate enablement under § 112(a).

However, to rigidly use the "representative number of examples" sub-test as the *only* test is incorrect. Just as the "teaching, suggestion, or motivation" test for obviousness this Court rejected in *KSR*, or the "machine or transformation" test for patent eligibility this Court rejected in *Bilski*, the "representativeness" test may have "captured a helpful insight," *KSR*, 550 U.S. at 418, and it may serve as "a useful and important clue," *Bilski*, 561 U.S. at 604. But "[h]elpful insights . . . need not become rigid and mandatory formulas." *KSR*, 550 U.S. at 419. The "representative number of examples" inquiry, in other words, may inform the § 112 analysis, but it "is not the sole test." *Bilski*, 561 U.S. at 604. The Federal Circuit erred in concluding that it was.

CONCLUSION

The Federal Circuit's current approach to § 112(a) fails to afford inventors of antibody-based therapies and other biotechnology inventions sufficient patent protection. If that approach is allowed to persist, the innovators in this field, who have invested tremendous amounts of time and money in research and development of such therapies, will find themselves increasingly exposed to free-riders. The free-riders will have invested minimal time and money but can quickly take

advantage of the innovators' underlying inventions and make copycat antibodies that either (i) do not infringe (in the case of narrow claims) or (ii) effectively invalidate the patent by rendering the specification's disclosure inadequately "representative" (in the case of broad claims). The copycat antibodies made by these free-riders do not represent any meaningful advancement in the art. Thus, the current regime encourages rote and conventional copying of already-existing therapies — not true innovation.

The Federal Circuit's approach also threatens to incentivize innovators in this field to avoid disclosing in their patent filings discoveries of the targets and pathways that underlie their inventions, and instead to patent one or a few specific antibodies through narrow, sequence-specific claims, without referencing the target. Such use of trade secrecy — even if temporary — will harm the transparency needed for future research and development in this promising area.

In short, the Federal Circuit's written-description jurisprudence frustrates both goals of the patent laws: it impedes incentives for innovation, and it discourages disclosures of broad inventions to the public. The result leaves everyone worse off — most of all, the patients who need these lifesaving therapies.

For these reasons, amici respectfully request that the Court grant certiorari and reverse the decision below.

Respectfully submitted,

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