NO. 21-757

In the
Supreme Court of the United States

AMGEN INC., et al.,

Petitioners,

v.

SANOFI, et al.,

Respondents.

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

BRIEF FOR RESPONDENTS

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QUESTION PRESENTED

The Patent Act requires a patent to disclose sufficient information about the claimed invention "to enable any person skilled in the art ... to make and use the same." 35 U.S.C. §112(a). The patents in suit here claim a broad genus of potentially millions of antibodies solely by the function they perform. Applying longstanding precedent unchallenged in this Court, the Federal Circuit held that the patents are invalid as a matter of law because they fail to teach a skilled person how to make and use the full scope of the claimed genus without undue experimentation.

The Court granted certiorari limited to the following question presented:

Whether enablement is governed by the statutory requirement that the specification teach those skilled in the art to "make and use" the claimed invention, 35 U.S.C. §112, or whether it must instead enable those skilled in the art "*to reach the full scope* of claimed embodiments" without undue experimentation—*i.e.*, to cumulatively identify and make all or nearly all embodiments of the invention without substantial "'time and effort,'" Pet.App.14a (emphasis added).

PARTIES TO THE PROCEEDINGS AND CORPORATE DISCLOSURE STATEMENT

Pursuant to this Court's Rules 24.1(b), 24.2, and 29.6, Respondents Sanofi, Aventisub LLC, f/k/a Aventis Pharmaceuticals Inc., Regeneron Pharmaceuticals, Inc., and Sanofi-Aventis U.S. LLC (Sanofi/Regeneron) state that the list of parties to the proceedings below in the brief on the merits by Petitioners Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc. (Amgen) is accurate. Sanofi/Regeneron further states that the corporate disclosure statement in their brief in opposition to certiorari remains accurate.[1]

[1] Sanofi (initially Aventis) and Regeneron have been full partners in developing the pharmaceutical at issue in this case. Accordingly, for brevity, this brief refers to them as "Sanofi/Regeneron," except where only one company undertook a particular activity. Sanofi and Regeneron did not jointly undertake every single activity that this brief attributes to "Sanofi/Regeneron," but the few such instances are immaterial for purposes of this case.

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INTRODUCTION

This case involves a patent dispute between innovators who independently developed antibody drugs that reduce low-density lipoprotein (LDL), or "bad," cholesterol. The antibodies bind to a protein, PCSK9, thus preventing the destruction of receptors that extract cholesterol from the bloodstream. Both the utility of discovering a PCSK9-inhibiting antibody and the time-and-labor-intensive methods for generating candidate antibodies were well known in the field, and multiple companies pursued an antibody with the desired characteristics. Sanofi/Regeneron developed Praluent, the first FDA-approved PCSK9 antibody, and Amgen developed Repatha. These antibodies differ substantially in their amino-acid sequences and where they bind to PCSK9. Both are used to treat tens of thousands of patients, but only Praluent is FDA-approved in a low-dose version, with no available substitute.

Each company patented its respective antibody by amino-acid sequence, the long-accepted way to claim a biological discovery. But years later, in a blatant attempt to corner the market—and *after* Sanofi/Regeneron developed Praluent and other companies developed their own antibodies—Amgen obtained *additional* patents that broadly claim *the entire genus* of PCSK9-blocking antibodies by function, rather than structure. Those are the patents at issue here, as Amgen asserted these broad, functionally-defined genus claims to literally try to take Praluent off the market and away from patients.

The Federal Circuit rightly rejected this gambit, holding that Amgen's broad functional genus claims

are not enabled and thereby invalid under 35 U.S.C. §112. While Amgen repeatedly derides the Federal Circuit's test as atextual, the requirement that a patent must provide sufficient disclosure to enable any skilled artisan to make and use the full scope of the claimed invention without undue experimentation is fully grounded in the text of §112 and this Court's cases. Indeed, Amgen ultimately embraces the "undue experimentation" standard and virtually the entire corpus of Federal Circuit decisions preceding the decision below, even though the words "undue experimentation" do not appear in §112. Instead, Amgen spends most of its brief assailing the Federal Circuit's purported cumulative-effort standard, even though the word "cumulative" does not appear in the decision below.

Amgen misleadingly suggests that the Federal Circuit acknowledged adopting a novel test that raised the bar and erected high hurdles. In reality, the Federal Circuit simply pointed out that Amgen itself raised the bar and created its own high hurdles by asserting a monopoly over an entire genus of functionally-defined claims. Those observations are hardly novel. This Court has long embraced the commonsense proposition that the more companies claim as their patent monopoly, the more they must enable. That is the heart of the patent bargain. Thus, no one suggests that Amgen's Repatha-specific patent has an enablement problem; it tells every skilled artisan how to make and use that innovation every time. But Amgen's effort to lay claim to an entire genus of functionally-defined antibodies is another matter entirely. The patents do not enable skilled artisans to make and use anything like the full scope

of the claimed genus, or any specific antibody within that genus (other than the relatively few antibodies whose structures are disclosed), or even entire classes of claimed antibodies with particular characteristics (*e.g.*, antibodies binding to more than nine of the sixteen identified PCSK9 amino acids). Indeed, the specification here tells skilled artisans little they did not already know, instead instructing them to make claimed antibodies by randomly generating and testing candidates via processes well-established in the prior art.

It is thus hardly surprising that both courts below, including the district court applying settled Federal Circuit precedent that Amgen accepts, had little difficulty rejecting Amgen's broad claims. The simple reality is that Amgen has claimed a monopoly over far more than it has enabled. Such claims are not just invalid, but dangerous. They can take medicines away from physicians and patients and could allow someone without a clinically valid species to claim an entire genus of medically-vital antibodies they have not yet discovered. This Court should affirm.

STATEMENT OF THE CASE

A. Statutory Background

The federal patent system "embodies a carefully crafted bargain" whose "ultimate goal" is "to bring new designs and technologies into the public domain through disclosure." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 150-51 (1989). To achieve that goal, the Patent Act offers inventors a "quid pro quo": a patentee obtains the "right of exclusion," but only in return for "full disclosure" of

"the invention." *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480-81, 484 (1974).

Chief among the disclosure requirements for a patent is §112's "enablement" requirement, which requires an inventor to disclose "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." 35 U.S.C. §112(a). The enablement requirement ensures that the public receives its side of the patent bargain; once the exclusivity period ends, "the knowledge of the invention inures to the people, who are thus enabled without restriction to practice it and profit by its use." *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 187 (1933). Equally important, the enablement requirement prevents over-claiming, ensuring that a patentee "can lawfully claim only what he has invented and described," and preventing patentees from foreclosing the future by claiming exclusive rights to discoveries not yet made. *O'Reilly v. Morse*, 56 U.S. (15 How.) 62, 121 (1854).

The enablement requirement now embodied in §112 has remained largely unchanged since the first Patent Act of 1790, which required a patent to contain a "specification in writing, containing a description … of the thing or things … invented or discovered … so particular" as to "enable a … person skilled in the art … to make, construct, or use" the invention. Act of Apr. 10, 1790, ch. 7, §2, 1 Stat. 109, 110-11. Beginning in the nineteenth century, this Court held that a patent is not enabled and thus void if a skilled person cannot make or use the claimed invention without

"painstaking experimentation," *Consol. Elec. Light Co. v. McKeesport Light Co.* (*The Incandescent Lamp Patent*), 159 U.S. 465, 474-75 (1895), or "elaborate experimentation," *Holland Furniture Co. v. Perkins Glue Co.*, 277 U.S. 245, 256-57 (1928). This rule was adopted by the regional circuits, *see, e.g.*, *Nat'l Theatre Supply Co. v. Da-Lite Screen Co.*, 86 F.2d 454, 455 (7th Cir. 1936), and by the United States Court of Customs and Patent Appeals (CCPA), which described that test as invalidating patents that required "undue experimentation," *e.g.*, *In re Folkers*, 344 F.2d 970, 976 (C.C.P.A. 1965).

The CCPA's successor, the Federal Circuit, likewise adopted this approach. In *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the Federal Circuit viewed it as "well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation." *Id.* at 737. The court set forth factors for "determining whether a disclosure would require undue experimentation" in order to "fully enable[]" an invention: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 736-37.

Current Federal Circuit law has distilled the foregoing principles into a straightforward enablement standard: "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the

claimed invention without 'undue experimentation.'" *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012). The enablement requirement is not a high hurdle for patents with tightly circumscribed claims, such as patents claiming particular antibodies by their structure, *i.e.*, amino-acid sequence. But, applying the "undue experimentation" standard and the *Wands* factors, the Federal Circuit has consistently held that a patent is not enabled if a claim encompasses "thousands" of "candidate compounds," and "testing" or "screening" of each candidate is necessary "to determine which … meet [the] claim." *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1156-58, 1162-63 (Fed. Cir. 2019); *see also Enzo Life Scis., Inc. v. Roche Molecular Sys., Inc.*, 928 F.3d 1340, 1345-49 (Fed. Cir. 2019); *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384-86 (Fed. Cir. 2013).

B. Factual Background

High LDL cholesterol (LDL-C) is a potential killer. It can cause cardiovascular disease, heart attacks, and strokes. *See Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1371 (Fed. Cir. 2017). Small molecule drugs (statins) can combat high LDL-C but can have adverse side effects or be ineffective for some patients. *Id.* One alternative treatment is a PCSK9 inhibitor.

PCSK9 is "a naturally occurring protein that binds to and causes the destruction of liver cell receptors … responsible for extracting LDL-C from the bloodstream." *Id.* As early as 1975, University of Texas–Southwestern researchers had discovered an inverse relationship between LDL receptors and cholesterol levels. C.A.App.3680-81. In 2001,

researchers discovered the gene that encodes PCSK9, though PCSK9's precise function remained unclear. C.A.App.3681. In 2006, UT–Southwestern researchers demonstrated that PCSK9 binds to and causes the destruction of LDL receptors that extract LDL cholesterol from the bloodstream, and proposed that antibodies could prevent PCSK9 from destroying the salutary LDL receptors. C.A.App.3681; *see* Jay D. Horton et al., *Molecular Biology of PCSK9: Its Role in LDL Metabolism*, TRENDS BIOCHEM SCI. 2007 February 32(2): 71–77.

Spurred by that publicly available research, several companies—including Amgen, Regeneron, Pfizer, and Merck—simultaneously and independently sought to create antibodies that could block PCSK9 from binding to LDL receptors, thereby sparing LDL receptors from destruction. C.A.App.3681, 3766. Antibodies are proteins that bind to target molecules ("antigens") like PCSK9. C.A.App.3679, 3693. An antibody is comprised of amino-acid chains, C.A.App.3679-80, which determine the antibody's three-dimensional structure and its antigen-binding features. C.A.App.3783; *see* C.A.App.3748; *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1290-91, 1301 (Fed. Cir. 2014).

To find cholesterol-lowering PCSK9 antibodies, Regeneron, like its rivals, used well-understood but resource-intensive methodologies for generating antibodies with desired qualities. It immunized mice, generated about 1,500 candidate antibodies, narrowed that pool to 35 antibodies for amino-acid sequencing, and ultimately identified a handful of antibodies that

bound to PCSK9 and blocked PCSK9 from binding to LDL receptors. C.A.App.3766. Sanofi/Regeneron proceeded with clinical development of one particularly promising antibody, alirocumab. *See Amgen*, 872 F.3d at 1372. In December 2008, Regeneron filed a provisional application that led to the issuance of a patent in November 2011 claiming alirocumab by its amino-acid sequence. *Id.*; *see* U.S. Patent No. 8,062,640; Prov. Appl. No. 61/122,482.

To get its PCSK9 inhibitor alirocumab to patients faster, Sanofi/Regeneron purchased a congressionally-authorized "priority review voucher" to expedite FDA review. *See* 21 U.S.C. §360ff. FDA approved alirocumab in July 2015, making alirocumab—marketed as Praluent—the first PCSK9 inhibitor available to patients in the United States. *Amgen*, 872 F.3d at 1372; C.A.App.3674.

Praluent successfully "targets PCSK9 to prevent it from binding to and destroying" LDL receptors, permitting the LDL receptors to "extract LDL-C thereby lowering overall LDL-C levels." *Amgen*, 872 F.3d at 1372. FDA approved Praluent in two doses: a 75-mg biweekly "low dose" that reduces LDL-C by approximately 45 percent, and a 150-mg biweekly "high dose" that reduces LDL-C by approximately 60 percent. *See* D.Ct.Dkt.349 at 295; D.Ct.Dkt.967, Ex.63, at 1 (Praluent label), *current version available at* https://bit.ly/3GSzvXQ.[2]

Amgen used similar techniques to develop its own PCSK9 antibody, designated 21B12, also known as

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[2] "D.Ct.Dkt." refers to district court docket entries, No. 14-cv-1317 (D. Del.).

evolocumab. *Amgen*, 872 F.3d at 1371. Amgen filed a patent application claiming 21B12/evolocumab by its amino-acid sequence that was published in February 2009 (two months *after* Regeneron filed its provisional patent application on alirocumab), and the patent issued in October 2011. *See id.*; U.S. Patent No. 8,030,457 ('457 patent). Amgen obtained FDA approval for evolocumab—marketed as Repatha—in August 2015, after Praluent was already on the market. *Amgen*, 872 F.3d at 1371. Unlike Praluent, Repatha lacks a low-dose version, and is approved only in 140-mg biweekly and 420-mg monthly doses, both of which reduce LDL-C by about 60 percent. *See* Dkt.967, Ex.64, at 1 (Repatha label), *current version available at* https://bit.ly/3knHQLr.

During the same period, Pfizer and Merck also used well-established techniques to develop their own PCSK9 antibodies. C.A.App.3681. Pfizer and Merck filed their first provisional patent applications on their PCSK9 antibodies in September 2008 and February 2008, respectively—preceding Amgen's public disclosure of its PCSK9 antibodies in February 2009—and obtained patents by amino-acid sequence. *See* Prov. Appl. No. 61/096,716, U.S. Patent No. 8,080,243 (Pfizer); Prov. Appl. No. 61/063,949, U.S. Patent No. 8,188,234 (Merck). Pfizer and Merck ultimately did not obtain FDA approval to market their antibodies, however, in Pfizer's case because of difficulties arising in clinical testing.

C. The Patents-In-Suit

This case does *not* involve Amgen's '457 patent claiming Repatha by its amino-acid sequence—the invention that Amgen purportedly "invested billions of

dollars and a decade of research bringing … to market." Br.7. That patent is fully enabled, and Praluent indisputably does not infringe it. Instead, this case involves two *additional* patents that Amgen obtained three years later, based on applications filed in 2013 and 2014, well *after* Regeneron had developed and patented Praluent. C.A.App.37, 421.

Unlike Amgen's '457 patent, which claimed Repatha's specific antibody by its amino-acid sequence, Amgen's new patents included broad, functionally-defined claims covering "the entire genus of antibodies that bind to specific amino acid residues on PCSK9 and block PCSK9 from binding to" LDL receptors. *Amgen*, 872 F.3d at 1372; *see* Pet.App.4a-5a; U.S. Patent Nos. 8,829,165 ('165 patent), 8,859,741 ('741 patent).[3] Put differently, rather than claim an antibody by *structure* (as with its '457 Repatha-specific patent, Regeneron's Praluent-specific patent, and the Merck and Pfizer patents), Amgen's later patents claim *all* antibodies with the *functions* of (i) binding to particular PCSK9 residues and (ii) blocking PCSK9 from binding to LDL receptors, regardless of whether Amgen could even make (let alone teach others to make) those antibodies.

Claim 19 of the '165 patent is representative of the asserted claims. That claim and its corresponding independent claim state:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following

[3] A "residue" is a particular amino acid in an amino-acid sequence. *Amgen*, 872 F.3d at 1372 n.3.

> residues [followed by a list of 15 amino acid residues], and wherein the monoclonal antibody blocks binding of PCSK9 to [LDL receptors].
>
> 19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues [followed by the same list of 15 amino acid residues as in claim 1].

Pet.App.4a.[4]

The '165 and '741 patents share a common specification, which describes the "trial-and-error process" that Amgen "used to generate and screen antibodies that bind to PCSK9 and block PCSK9 from binding to" LDL receptors. *Amgen*, 872 F.3d at 1372; Pet.App.3a. The specification sets forth two methods to search for claimed antibodies, both of which require making new antibodies and testing them to determine if they possess the recited binding and blocking functions and thus fall within the claims' scope. The first method is to randomly generate pools of antibodies by immunizing a mouse or using phage display. C.A.App.223-25, 234-38, 3908-09. The second method is to make amino-acid substitutions to disclosed antibodies, as suggested by the specification's Table 1. C.A.App.211.

The specification discloses the amino-acid sequences of 26 antibodies that (according to Amgen) bind to PCSK9 and block the binding of LDL receptors, thus falling within the claims' scope. C.A.App.51-116,

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[4] The '741 patent's claim recites another PCSK9 residue, making the total number of residues sixteen.

240, 3868; *Amgen*, 872 F.3d at 1372. The specification provides the three-dimensional structure—showing how the antibody actually binds to PCSK9—for just two. C.A.App.247-49; *Amgen*, 872 F.3d at 1372.

D. Proceedings Below

In October 2014, mere days after obtaining its new '165 and '741 patents, Amgen sued Sanofi/Regeneron for infringement, asserting that Praluent fell within the broad functional genus claimed. Pet.App.5a. Given the breadth of those claims, Sanofi/Regeneron stipulated to infringement, but argued (as relevant here) that the '165 and '741 patents are invalid for failure to satisfy the enablement requirement. Pet.App.5a; *Amgen*, 872 F.3d at 1372.

1. First trial and appeal

A jury ruled for Amgen, and the district court granted a permanent injunction removing Praluent from the market. *Amgen*, 872 F.3d at 1372-73. The Federal Circuit entered a stay before the injunction took effect, and on appeal, Sanofi/Regeneron emphasized that the district court erroneously excluded important evidence showing that even after Amgen filed its patent application, it continued its trial-and-error search for antibodies within the genus, thus underscoring that the specification was inadequate to enable the claimed invention. Sanofi/Regeneron also contended that the court had erroneously instructed the jury that it could find that Amgen satisfied §112's related written-description requirement if the specification disclosed a "newly characterized antigen." *Id.* at 1376.

The Federal Circuit unanimously agreed with both arguments, vacated the jury verdict and permanent injunction, and remanded for a new trial on enablement and written description. *Id.* at 1371, 1381-82. Amgen petitioned for certiorari, arguing that in evaluating written description, the Federal Circuit employs a "self-created 'possession' standard" rather than the text of §112. Pet.2, *Amgen, Inc. v. Sanofi*, No. 18-127 (U.S. July 23, 2018). In contrast to that allegedly "court-made" standard, *id.* at 34, Amgen told this Court that "[f]or enablement, the Federal Circuit applies the statutory standard." *Id.* at 3. The Court denied certiorari. *See* 139 S.Ct. 787 (2019).

2. Second trial

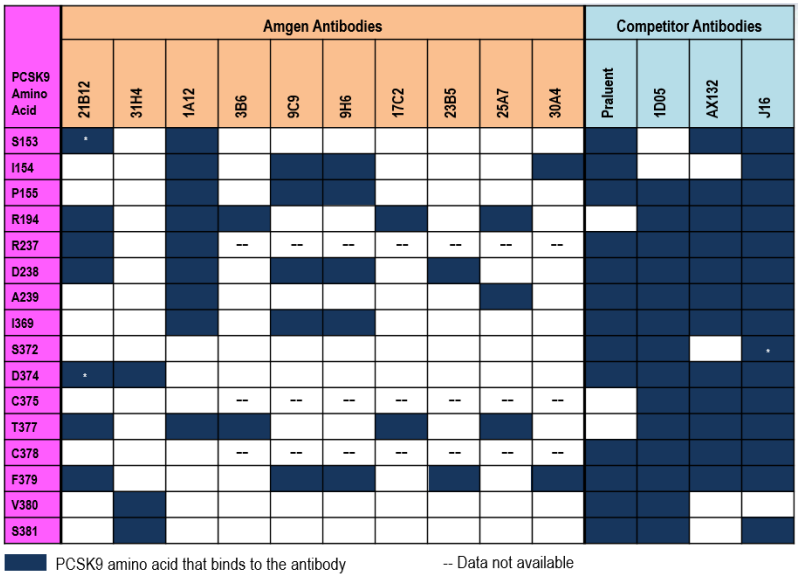
On remand, the case was reassigned to a new trial judge. Before trial, Amgen again succeeded in excluding evidence showing that for years after the patents' filing date, Amgen tried and failed to generate certain desirable antibodies (called "EGFa mimics") within the claims of the '165 and '741 patents via trial and error—thus showing that the patents did not enable a skilled person, or even the purported inventor, to make and use the claimed genus. *See* C.A.App.3686-87, 3807-08, 3869-70, 5428-31.

Despite being hamstrung by that evidentiary ruling, Sanofi/Regeneron presented undisputed evidence demonstrating that Amgen's patents do not enable the genus that Amgen claimed, including expert testimony that the patents "cover … a vast scope of possible antibodies," potentially "millions," and implicate "an astronomically large number" of candidates. C.A.App.3750, 3688, 3759. Amgen's witnesses did not disagree; they were unable even to

estimate the number of antibodies within the claims' scope, *e.g.,* C.A.App.3869, with one agreeing that following the patents' teaching would generate "millions and millions" of candidates, C.A.App.3902. The evidence showed that the immunization method that Amgen's patents disclosed was "like a fishing expedition": the natural "randomness in how the immune system" produces antibodies means that each immunization creates a "big pool of potential [antibodies]," and "you don't know what you're going to get." C.A.App.3689-90. Given that randomness, a skilled artisan "could be immunizing mice for a hundred years" and still not create a particular desired antibody. C.A.App.3754.

Amgen's witnesses conceded that given the unpredictability of antibody science, a skilled artisan would have to test every single antibody generated by the methods disclosed in Amgen's patents to determine whether it has the necessary functional properties to fall within the claimed genus; accordingly, a skilled artisan cannot use those methods to identify and create a specific new antibody within the claims' scope, such as Praluent or the Pfizer/Merck antibodies. As one Amgen expert testified, knowing "the amino acid sequence of an antibody" does not "tell you the property of where it binds," so to determine if each generated antibody would actually bind PCSK9 and block, "you'd have to test" it. C.A.App.3914-18. An Amgen inventor likewise admitted that even "conservative" substitutions—*i.e.*, changing one amino acid of an antibody disclosed in the patent—are unpredictable and require testing. C.A.App.3768-69.

Sanofi/Regeneron also presented undisputed evidence that the antibodies disclosed in Amgen's patents were not representative of or structurally similar to four antibodies (including Praluent) discovered by Amgen's competitors and known to fall within the claims—much less to the millions of additional antibodies that the claims encompass. For example, Sanofi/Regeneron showed that those four antibodies bound to PCSK9 at more, and markedly different, residues than Amgen's disclosed antibodies:



C.A.App.4283; C.A.App.3692.[5] The jury found two of the five asserted claims invalid for insufficient written description, but found for Amgen on the three remaining claims. Pet.App.18a-19a.

[5] "1D05" and "AX132" are Merck's antibodies; "J16" is Pfizer's antibody.

Sanofi/Regeneron moved for judgment as a matter of law on enablement (and written description). Sanofi/Regeneron argued that, under *Wands*, making and using the "full scope" of Amgen's claimed genus required "undue experimentation." In its opposition, Amgen did not dispute the relevant standard for evaluating enablement but embraced it, contending that, on the facts, "the *Wands* factors establish that practicing the full scope of the claims does not require undue experimentation." D.Ct.Dkt.923 at 14 (capitalization altered). It argued that "the specification provides a detailed 'roadmap' enabling … the *full* scope of the claims without undue experimentation." *Id.* (Amgen's emphasis).

The district court granted JMOL on enablement. Applying the *Wands* factors to the record evidence, as Amgen had urged, the court concluded that Amgen's patents require undue experimentation and thus are not enabled. Pet.App.27a-44a. Among other things, the court determined that "a reasonable factfinder could only conclude on this factual record" that "the scope of the claims is vast"; "the art is unpredictable"; and the patent "do[es] not teach a person of ordinary skill in the art how to predict from an antibody's sequence whether it will bind to specific PCSK9 residues" or how to "discover undisclosed claimed embodiments." Pet.App.34a, 35a-38a, 40a-41a. Accordingly, "any reasonable factfinder would find that practicing the claims' full scope" would require "undue experimentation." Pet.App.43a-44a.

3. Second appeal

a. Amgen appealed to the Federal Circuit. As in the district court, Amgen did not challenge the Federal

Circuit's enablement standard. Instead, Amgen argued: "The enablement requirement is satisfied if the specification teaches [skilled persons] 'how to make and use the full scope of the claimed invention without "undue experimentation."'" Amgen.C.A.Br.31 (quoting *MagSil,* 687 F.3d at 1380); *accord id.* at 34. Amgen principally contended that the district court had erred in applying the Federal Circuit's long-established enablement standard to the record evidence. *See id.* at 32-63. Only at the end of its brief did Amgen contend that the district court erred by construing the "full scope" requirement as requiring Amgen to make "*every antibody* within the scope of the claims." *Id.* at 64 (Amgen's emphasis). That interpretation, Amgen argued, was contrary to Federal Circuit precedent, which "does *not* require the patent to 'describe how to make and use every possible variant.'" *Id.* (Amgen's emphasis).

The Federal Circuit unanimously affirmed. Pet.App.1a-15a. The court set forth §112's text and observed that the enablement requirement is intended "to ensure that the public is told how to carry out the invention, *i.e.*, to make and use it." Pet.App.6a. In light of the statute's text and purpose, a patent's disclosure must be "commensurate with the scope of the claims," such that "when a range is claimed," the patentee must enable "the scope of the range." Pet.App.7a-8a. As a result, claims with "broad functional language" may create "high hurdles in fulfilling the enablement requirement" given the need to enable the "full scope" of what is claimed without undue experimentation. Pet.App.11a-12a.

"[W]eighing the *Wands* factors," the Federal Circuit held that "undue experimentation would be required to practice the full scope of [Amgen's] claims." Pet.App.15a. The court observed that Amgen's functionally-defined genus claims "were indisputably broad," and "far broader in functional diversity than the disclosed examples." Pet.App.12a-13a. The court also observed—citing Amgen's own witnesses—that the "field of science" was "unpredictable," noting the "absence of nonconclusory evidence that the full scope of the broad claims can predictably be generated by the described methods." Pet.App.13a. Thus, any reasonable factfinder would conclude that the specification "does not provide significant guidance or direction to a [skilled] person … for the full scope of the claims," as there was no "adequate guidance beyond the narrow scope of the working examples that the patent's 'roadmap' produce[s]." Pet.App.14a; *see* Pet.App.13a n.1 ("[A]lthough the claims include antibodies that bind up to sixteen residues, none of Amgen's examples binds more than nine."). In the court's view, "[t]he facts of this case" were "analogous to those" in its recent *Idenix*, *Wyeth*, and *Enzo* decisions. Pet.App.15a. Throughout its decision, the Federal Circuit repeatedly eschewed bright-line rules or tests. *See* Pet.App.12a ("functional claim limitations are not necessarily precluded in claims that meet the enablement requirement"); Pet.App.13a ("some need for testing by itself might not indicate a lack of enablement"); Pet.App.14a ("We do not hold that the effort required to exhaust a genus is dispositive.").

b. Amgen sought rehearing en banc, contending that the panel had "announce[d] a new test" for

enablement that evaluated the "'time and effort'" required "'to reach the full scope of claimed embodiments.'" Amgen.C.A.Reh'g.Pet.1 (quoting Pet.App.14a) (emphases omitted). The Federal Circuit denied the petition without dissent. Pet.App.60a-61a.

The panel issued an opinion respecting denial, explicitly rejecting Amgen's assertion that its decision "created a new test for enablement." Pet.App.62a. The panel explained that its decision "specifically resisted" any cumulative-effort "numerosity" or "exhaustion" requirement. Pet.App.64a. Instead, the panel explained, the test for enablement is and "has always been" that the patent "must enable [the] invention, whatever the invention is." Pet.App.62a. There is no special rule for functional or genus claims, but the more that is claimed, the more that must be enabled. Pet.App.62a-63a. That standard ensures that a patentee cannot obtain "protection for inventions broader than are disclosed or enabled, and that were apparently not invented by the applicant." Pet.App.64a. An inventor who "has disclosed or enabled only a small number of invented species ... has not invented a broad genus." Pet.App.64a.

The problem with Amgen's patents, the panel emphasized, is "not that it would take a long time to collect the full set of each and every embodiment." Pet.App.65a. Rather, the problem is that "the narrow and limited guidance in the specification" leaves countless undisclosed embodiments "inaccessible or uncertain to make." Pet.App.65a.

SUMMARY OF ARGUMENT

The decision below follows directly from statutory text and settled precedent and should be affirmed. Under §112, a patent must disclose enough to "enable any person skilled in the art ... to make and use the [invention]." 35 U.S.C. §112(a). As more than a century of this Court's cases show, that standard has long been understood to require sufficient disclosure to enable a skilled artisan to make the entire invention claimed, not just a subset, without the need for any significant independent experimentation. Consistent with statutory text and the basic "patent bargain," the more that is claimed as a monopoly for the inventor, the more that must be enabled for skilled artisans in the field. That commonsense standard precludes someone from claiming a broad functionally-defined genus without enabling skilled artisans to predictably generate specific embodiments absent "undue experimentation," let alone, as here, leaving skilled artisans with no practical guidance for creating particular undisclosed embodiments beyond what they had before reading the specification.

Amgen has no meaningful response to that settled law—which it embraced below. Instead, Amgen devotes most of its brief—from its Question Presented onward—to attacking a straw man, by asserting that the Federal Circuit's decision adopted a novel enablement standard that turns on the effort required to "cumulatively identify and make all or nearly all embodiments of the invention." That phrase is repeatedly introduced by an "*i.e.*"—a tell that it is a flat mischaracterization of the Federal Circuit's

decision, which neither uses the word "cumulative" nor endorses any such cumulative-effort test.

While Amgen criticizes the Federal Circuit for purportedly adding extratextual requirements, its own proposed "as-needed" standard is the one that introduces words that are not in the text and introduces concepts that are foreign to this Court's caselaw. There is simply no grounding in text or precedent for an as-needed standard or for allowing companies to monopolize far more than they enable.

In fact, Amgen's approach would have serious negative consequences for future innovation. Despite Amgen's sky-is-falling lamentations, innovation has not been harmed by the decision below, as Amgen's leading academic article ultimately concedes. Rather, the true threat to innovation comes from allowing companies to monopolize an entire functional genus that they have not enabled. This case amply demonstrates that danger, as Amgen seeks to remove the only FDA-approved low-dose PCSK9 antibody from the market. Worse still, Pfizer's experience demonstrates the risk that someone could monopolize an entire genus without having a medically viable species that survives clinical testing, leaving patients without needed treatment.

Finally, the flaws in Amgen's specification are fundamental and would fail any viable test for enablement. The problem here is not that Amgen's specification leaves some small hole in the genus unenabled or requires some modest gap to be filled in by experimentation. Instead, the specification is useless in enabling a skilled artisan to generate any specific undisclosed antibody within the genus,

including entire classes of claimed antibodies (such as those binding to more than nine identified residues). Rather, the specification leaves skilled artisans seeking to make and use desired undisclosed embodiments exactly where they started—consigned to use well-understood techniques to generate antibodies by trial and error without any ability to determine whether they even fall within the claimed genus without doing further testing. In sum, Amgen has claimed far more than it has enabled, and two courts have correctly invalidated the patents applying well-established and textually grounded tests. This Court should follow suit and affirm.

ARGUMENT

I. The Federal Circuit's Enablement Standard Is Faithful To Section 112's Text And This Court's Precedents And Was Properly Applied Here.

A. Section 112 and This Court's Decisions Require Enablement of the Full Scope of a Claim Without Elaborate Experimentation.

To obtain a patent, §112 requires an applicant to provide "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." 35 U.S.C. §112(a). This "enablement" requirement is "'the quid pro quo of the right to exclude'" in the basic patent bargain. *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc.,* 534 U.S. 124, 142 (2001); *see also Pennock v. Dialogue*, 27 U.S. 1, 23 (1829) (Story, J.) (discussing this "quid pro quo").

"[E]xclusive patent rights are given in exchange for disclosing the invention to the public." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 736 (2002).

The requirement of an enabling disclosure in exchange for a patent monopoly is not new; it traces back to pre-Framing English precedent. In *King v. Arkwright*, Justice Buller explained that "to entitle himself to the benefit of a patent for a monopoly," an inventor "must disclose his secret, and specify his invention in such a way, that others may be taught by it to do the thing for which the patent is granted." Dav. Pat. Cas. 61, 106, Webs. Pat. Cas. 64, 66 (K.B. 1785). That understanding crossed the Atlantic and was reflected in the first Patent Act, which required "a specification in writing, containing a description … of the thing or things … invented or discovered … so particular … as … to enable a … person skilled in the art … to make, construct, or use the same, to the end that the public may have the full benefit thereof, after the expiration of the patent term." Patent Act of 1790, §2, 1 Stat. at 110. Subsequent Patent Acts contained similar language, as does the current §112. *See, e.g.*, Patent Act of 1836, ch.357, §6, 5 Stat. 117, 119 (requiring "description of his invention … in such full, clear, and exact terms to enable any person… to make … and use the same"); Patent Act of 1870, ch.230, §26, 16 Stat. 198, 201.

Section 112 and its predecessors have consistently required a "full, clear, concise and exact" disclosure that enables a skilled artisan to "make and use" the "invention"—not just a subset of the invention. Under the first Patent Act, one who invented a "thing or

things" had to enable "the same"; one could not obtain a monopoly over "things" while enabling only a "thing." Later versions similarly demanded enablement of the invention in full, clear, and exact terms. This Court's cases reflect that clear text. The "quid pro quo" offered by the Patent Act is that a patentee obtains "a right of exclusion," but only in return for "*full disclosure*" of "*the invention*." *Kewanee*, 416 U.S. at 480-81, 484 (emphases added). The right to exclude attaches only after disclosure sufficient "to enable one skilled in the art to practice *the invention* once the period of the monopoly has expired." *Univ. Oil Prods. Co. v. Globe Oil & Refining Co.*, 322 U.S. 471, 484 (1944) (emphasis added).

The "invention" that must be enabled is defined by a patent's claims—a development that emerged in the mid-nineteenth century and is reflected in the text of §112. Under "early patent practice in the United States, … it was the written specification that represented the key to the patent." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 902 (2014). Eventually, however, patent applicants began to set out the invention's scope in a separate section known as the "claim." *Id.* In 1836, Congress required a patent applicant to provide a written description that "particularly specif[ied] and point[ed] out the part, improvement, or combination, which he claims as his own invention or discovery." *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 379 (1996). A separate claim became a statutory requirement in 1870. *Id.*; *see* 35 U.S.C. §112(b) (inventor must set out "one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor ... regards as the invention"). A patent's

claims "measure the invention," *Cont'l Paper Bag Co. v. E. Paper Bag Co.*, 210 U.S. 405, 419 (1908), and define the monopoly property right, *see Nautilus*, 572 U.S. at 901-02.

With the advent of claiming, some patent applicants, seeking to preempt more than they actually invented, began defining the scope of their patented inventions with overly broad language that exceeded the limited disclosures in their specifications. This Court consistently rejected such efforts to over-claim and under-disclose as contrary to the basic bargain underlying our patent system. In *O'Reilly v. Morse*, for instance, the Court upheld the validity of seven claims that were limited to telegraph structures and systems described in the patent. 56 U.S. at 85-86, 112. But the Court deemed "too broad" an eighth claim for the "use of the motive power of the electric or galvanic current, [called] electro-magnetism, … for marking or printing intelligible characters, signs, or letters, at any distances." *Id.* at 112-13. That "invention," the Court concluded, violated §112's predecessor because its scope went beyond the patent's disclosure. *Id.* at 113, 118-20.

Similarly, this Court routinely invalidated patents for non-enablement where the inventor claimed a whole class of embodiments characterized by function without commensurate disclosure. For example, in *Lamp*, the Court invalidated a claim to "the use of all fibrous and textile materials for the purpose of electric illuminations" where the patent left others to engage in "painstaking experimentation" among "different species of vegetable growth, for the purpose of ascertaining the one best adapted to an

incandescent conductor." 159 U.S. at 472-73, 475. In *Holland Furniture Co. v. Perkins Glue Co.*, the Court invalidated a claim to all starch glues functioning like animal glue because the patent described only "a particular starch glue" and finding others required "elaborate experimentation." 277 U.S. at 256-57. In *Béné v. Jeantet*, the Court invalidated a claim to a method of shrinking coarse hair by "subjecting it to the action of chemicals" because the patent merely disclosed one chemical "solution" and did not "enable" a skilled person "to use the invention without having to resort to experiments of his own to discover those [other] ingredients." 129 U.S. 683, 684-86 (1889). And in *Corona Cord Tire Co. v. Dovan Chemical Corp.*, the Court invalidated certain claims to a process for treating rubber by combining it with "a disubstituted guanidine." 276 U.S. 358, 385 (1928). The patent permissibly claimed diphenylguanidine as an accelerator, but went too far in claiming "other derivatives of guanidine in which two of the hydrogen atoms of guanidine nucleus have been substituted by other groups," because there were "between 50 and 100 substances" that fit that description and the patentee had not disclosed "any general quality common to disubstituted guanidines which made them all effective as accelerators." *Id.*

The Court has thus long recognized that a patent does not satisfy the enablement requirement if the specification does not allow skilled artisans to make or use the entire claimed invention without "painstaking experimentation," *Lamp*, 159 U.S. at 474-75, or "elaborate experimentation." *Holland*, 277 U.S. at 256-57. The Court's decisions reflect the commonsense principle that the more the inventor

claims, the more the specification must enable, and the commonsense corollary that when claims outstrip the accompanying disclosures, skilled artisans will be consigned to "painstaking experimentation" to make and use the full scope of the claimed invention and that such claims are invalid.

B. The Federal Circuit, in General and in the Decision Below, Requires No More Than the Statutory Text and This Court's Cases Demand.

The Federal Circuit's enablement standard faithfully embodies §112's text and this Court's precedents. In fact, the statutory text, this Court's cases, and a whole line of Federal Circuit precedents guard against what Amgen has done here: claim a lot and disclose a little, such that skilled artisans (and even Amgen's own scientists) must engage in undue experimentation because the disclosure leaves them guessing as to how to make and use the full scope of the claimed invention.

Consistent with this Court's decisions, the Federal Circuit's predecessor, the CCPA, "summed up" the §112 requirement as "whether the scope of enablement provided to one of ordinary skill in the art by the disclosure is such as to be commensurate with the scope of protection sought by the claims." *In re Moore*, 439 F.2d 1232, 1236 (C.C.P.A. 1971); *accord In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970). And it described the amount of experimentation warranting invalidation as "undue experimentation." *In re Folkers*, 344 F.2d 970, 976 (C.C.P.A. 1965); *see Fields v. Conover*, 443 F.2d 1386, 1390-91 (C.C.P.A. 1971) (holding that disclosure complies with §112 even if

"some experimentation" is required, "provided it is not an undue amount").

The Federal Circuit, in turn, has long recognized that a patent's disclosure must be "at least commensurate with the scope of the claims." *Crown Operations Int'l, Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1379 (Fed. Cir. 2002); *see In re Hyatt*, 708 F.2d 712, 714 (Fed. Cir. 1983) (stating that §112 requires "the enabling disclosure of the specification be commensurate in scope with the claim under consideration"). In the "seminal" *In re Wands* decision, Br.23, the Federal Circuit explained that "it is well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation," and it articulated eight factors for "determining whether a disclosure would require undue experimentation" in order to "fully enable[]" an invention. 858 F.2d at 736-37.

Reflecting the foregoing principles, the Federal Circuit has set forth a straightforward, administrable standard for enablement: "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *MagSil*, 687 F.3d at 1380; *see also McRO, Inc. v. Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020) ("Once the precise scope of the claimed invention is defined, the question is whether undue experimentation is required to make and use the full scope of embodiments of the invention claimed.").

In a series of cases, the Federal Circuit has applied this standard in the particular context of

evaluating whether genus claims with functional limitations were enabled, and it concluded that the claims lacked enablement due to "undue experimentation." That is not because the Federal Circuit applies a special rule to genus claims or functional claims or even functional genus claims, but because the more one claims, the more one must enable, and some genus claims assert a monopoly over far more than they enable. In *Idenix*, for example, the court held that the claims were not enabled after observing, *inter alia*, that there were "many, many thousands of candidate compounds"; "[t]esting" or "screening" of each candidate compound was necessary to determine whether it satisfied the claim's functional requirements, given the "unpredictability" of the art; and the specification only "contain[ed] some data showing working examples," leaving a skilled person to "'engage in an iterative, trial-and-error process to practice the claimed invention,'" even if "synthesis of an individual [compound] was largely routine." 941 F.3d at 1156-63. Similarly, in *Enzo*, the court held that the claims were not enabled given that the "number of possible" compounds within the claims was "at least 'tens of thousands,'" each of which "would need to be tested" to determine if it satisfied the functional requirements given "unpredictability in the art." 928 F.3d at 1346-49. And in *Wyeth*, the court held the claims invalid because there were potentially "tens of thousands of candidates," and the art was "unpredictable," since even "minor alterations" to a compound "could impact its" functional properties. 720 F.3d at 1384-86.

The Federal Circuit followed this precedent—all built on §112's text and this Court's decisions—in this

case, which likewise involves genus claims with functional limitations. The court noted that an enabling disclosure "must be at least commensurate with the scope of the claims." Pet.App.6a-7a. Accordingly, it explained, an inventor that "claims with broad functional language" faces "high hurdles" in "fulfilling the enablement requirement." Pet.App.12a; *see also* Pet.App.62a-63a (explaining that "[i]f the invention is a group of compositions, defined as a genus," it must be "enabled by a disclosure commensurate with the scope of the genus"). These observations are fully consistent with the requirement of §112's text that a specification enable the "invention" claimed and the commonsense principle that the more that is claimed, the more that must be enabled.

The court then "turn[ed] to the specific *Wands* factors" and concluded that "undue experimentation would be required to practice the full scope of" Amgen's functionally-defined genus claims. Pet.App.10a, 12a-15a. In so doing, the court determined that "the facts of this case are … analogous to those in" *Idenix*, *Enzo*, and *Wyeth*. Pet.App.15a. The Federal Circuit's decision was thus fully consistent with this Court's decisions in *Lamp*, *Holland*, *Béné*, and *Corona*, all of which invalidated genus claims requiring skilled artisans to make and test candidates to find embodiments beyond the relatively few disclosed in the patent.

II. Amgen Provides No Persuasive Reason To Establish A New Enablement Standard.

Amgen does not take issue with the vast majority of this corpus of precedent. Indeed, for all its rhetoric about extratextual requirements à la *Bilski*, Amgen does not challenge the "undue experimentation" standard, the *Wands* factors, or any broader aspect of Federal Circuit law, even though the text of §112 makes no reference to "undue experimentation," let alone the eight *Wands* factors. Amgen does not even dispute that the specification must "teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *MagSil*, 687 F.3d at 1380. Nor could it: Amgen embraced this same "full scope" standard in its briefing below, *see* Amgen.C.A.Br.31; it previously told this Court that, "[f]or enablement, the Federal Circuit applies the statutory standard," p.13, *supra*; and it acknowledges that a patent must "reasonably enable the entire scope of the claim," Br.28. Amgen similarly accepts the *Wands* factors as useful for determining whether "undue experimentation" is required to enable the full scope of the claimed invention. *See* Br.23 (describing *Wands* as "seminal"). Even more remarkably, Amgen does not take issue with the Federal Circuit's recent decisions in *Idenix* and *Wyeth*, even though the court invalidated the functional genus claims there based on the same kind of enablement problems that doom Amgen's patents.

Instead, Amgen spends practically its entire brief attacking a straw man, adding its own language to a passage in the decision below to claim that the Federal

Circuit adopted a novel enablement standard that turns on the effort required to "cumulatively identify and make all or nearly all embodiments of the invention." Br.i; *see* Br.2, 5, 18, 19, 27, 28. That assertion egregiously mischaracterizes the decision, which neither endorses nor relies on any such cumulative-effort standard—and in fact, expressly *rejects* it.

A. Amgen Mischaracterizes the Decision Below.

From its Question Presented to the last page of its brief, Amgen rests its case for reversal on a profound mischaracterization of the decision below. In Amgen's telling, the Federal Circuit erred by adopting a "new" and "different" enablement standard that "fundamentally alters the patent bargain" by making enablement depend on the effort required to "cumulatively identify and make all, or nearly all, possible variations of the invention." Br.2, 19-20, 24. Amgen spends a full 20 pages of its argument section attacking this standard as contrary to text, precedent, practice, and policy. Br.21-41.

There is a singular problem with that approach: The Federal Circuit has never endorsed or relied on any such cumulative-effort standard, as it made clear in both the decision below and its statement concerning rehearing when Amgen mischaracterized the decision in this way. The decision could hardly be clearer that it "*do*[*es*] *not hold* that the effort required to exhaust a genus is dispositive." Pet.App.14a (emphasis added); *see also, e.g.*, Pet.App.8a (patent need not "describe how to make and use every possible variant of the claimed invention"); Pet.App.13a

(enablement is "not concerned simply with the number of embodiments"). The panel underscored that point on rehearing, emphasizing that the decision "specifically resisted what might be termed a simple 'numerosity' or 'exhaustion' requirement," and that any assertion that the Federal Circuit had "adopted a 'numbers-based standard' to evaluate enablement" that asked "how long it would take to make and screen every species" simply "mischaracterizes our law." Pet.App.64a; *contra, e.g.*, Br.26 (asserting that the panel "turned enablement into a numbers game").

As the panel explained, the problem with Amgen's patents "*was not* that it would take a long time to collect the full set of each and every embodiment," Pet.App.65a (emphasis added), as would a claim that fully enables skilled artisans to predictably generate every embodiment but that would require substantial time to do so given the sheer number of embodiments. The problem was that the unpredictability of the science combined with a broad functional claim that "extend[ed] far beyond the examples and guidance provided" left skilled artisans with no ability to generate specific undisclosed embodiments and no option but to engage in trial and error using well-established techniques to generate candidate antibodies that would then still need to be tested to ascertain whether they came within the claimed genus. Pet.App.65a. The panel had little difficulty in concluding that this constituted "undue experimentation" under the *Wands* factors, which Amgen does not challenge. Pet.App.64a-65a.

Amgen points to no language in the Federal Circuit's opinion actually adopting the "cumulatively

identify and make all or nearly all embodiments" standard it assails. *Contra* Br.i, 2, 5, 18, 19, 27, 28. In fact, the word "cumulative" and its variants do not appear *once* in the decision below (despite appearing a dozen times in Amgen's brief). Instead, Amgen twists the Federal Circuit's words, transforming the phrase "reach the full scope of claimed embodiments"—which the Federal Circuit used exactly once, *see* Pet.App.14a—into "cumulatively identify and make all or nearly all embodiments of the invention." Br.i; *see, e.g.*, Br.2 ("'*reach the full scope* of claimed embodiments'—*i.e.*, to cumulatively identify and make all, or nearly all, possible variations"); Br.5 ("'*to reach* the full scope of claimed embodiments' ... *i.e.*, to cumulatively identify and make all or nearly all embodiments"); Br.18, 19, 27 (same). Amgen's repeated use of "*i.e.*" is a tell that the Federal Circuit never actually adopted a cumulative-effort test.

When a specification enables a skilled artisan to predictably make specific undisclosed embodiments under circumstances where making all of them would take time, the cumulative effort needed to make and use every single embodiment of the claimed invention is unproblematic. But when the specification provides no useful guidance to skilled artisans to make and use specific undisclosed embodiments and consigns them to a trial-and-error process to unpredictably generate antibodies that must then be tested to determine whether they even fall within the broad functionally-claimed genus, Federal Circuit precedent along with this Court's precedent and statutory text all indicate that the claimed invention is not enabled. Under those circumstances, the reality that even substantial effort will not allow skilled artisans "to practice the

full scope of these claims," Pet.App.15a, provides confirming evidence that the specification leaves skilled artisans in the dark. But, as the Federal Circuit was at pains to emphasize, that commonsense observation simply does not translate into a "cumulative effort" test that would condemn a patent that gives a skilled artisan clear guidance to make and use any undisclosed embodiment of the claim through a time-consuming process.

Amgen engages in similar distortion in asserting that the panel "acknowledged" it was adopting a "different standard" that "'raises the bar'" and imposes "'high hurdles in fulfilling the enablement requirement.'" *Contra* Br.2 (quoting Pet.App.12a-13a), Br.19-20, 24, 25. Instead, the panel simply observed correctly that Amgen had raised the bar on itself by claiming a broad functional genus. To state the obvious, there is no enablement problem with Amgen's '457 patent claiming Repatha by its amino-acid sequence or with Regeneron's claim to Praluent by its amino-acid sequence. A skilled artisan can make and use those structurally defined and adequately disclosed antibody inventions every time. The problem was introduced when Amgen tried to monopolize the whole field with broad functional claims that taught skilled artisans barely anything more than what they already knew—namely, that through trial and error using well-established techniques, they might be able to generate some antibodies within the claims. By claiming far more than the particular antibodies it had already discovered, and laying claim to an entire genus of functionally-defined antibodies (including antibodies that Amgen specifically sought but could not make),

Amgen "raised the bar" and created "high hurdles" for its specification. And Amgen's actual specification falls far short of the mark.

That in no way suggests (let alone "acknowledges") that the panel was adopting a "different standard" for functionally-defined genus claims. Instead, it simply reflects that under the longstanding statutory standard for enablement, the breadth of disclosure necessary to meet the enablement requirement depends on the breadth of the claimed invention: the more that the patent claims, the more it must enable. That principle has long been a feature of Federal Circuit law, *see*, *e.g.*, *MagSil*, 687 F.3d at 1381 ("[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage."), and has been applied in previous cases that Amgen accepts to require more of those who claim a broad functional genus, *see, e.g.*, *Idenix*, 941 F.3d at 1165.

B. To the Extent Amgen Is Proposing a New Enablement Standard, Its Standard Conflicts With Statutory Text, Settled Precedent, and Longstanding Practice.

While Amgen is reasonably clear in rejecting the strawman cumulative-effort test, it is decidedly less clear in explaining its own view of what §112's enablement standard actually requires. At times, it appears to embrace the standard that the Federal Circuit applied below (and in countless other cases) shorn of the imagined cumulative-effort standard. *See* Br.28 (specification must "reasonably enable the entire scope of the claim"); Br.43 (enablement requires disclosure "commensurate with the scope of protection

sought by the claims"). But that would lead to affirmance, as the Federal Circuit never used the word cumulative and disclaimed any cumulative-effort standard.

At other times, Amgen appears to espouse a substantially diluted test for enablement—a "practical" test that requires a patent to enable skilled artisans only to "put the claimed inventive concept into practice" in *some* way, "as needed," without necessarily enabling skilled artisans to make and use the full scope of the claimed invention. Br.29; *see* Br.3 ("how to 'make and use' the invention as needed"); Br.20-21 ("reasonably make and use individual embodiments *as needed*"); Br.28 ("produce and employ physical versions of the invention as needed"); Br.41 ("permit skilled artisans to practice claims as needed"). But it is entirely unclear where this as-needed standard comes from—certainly not the statutory text—or whose needs control. Moreover, this test elides the fundamental problem with the specification—namely that it provides no guidance to allow skilled artisans to predictably produce any specific undisclosed embodiment, let alone the full scope of the claimed invention. Simply put, Amgen's as-needed standard cannot be reconciled with statutory text, settled precedent, or longstanding practice.

1. The statutory text alone is conclusive. Section 112(b) explicitly requires a patent to "particularly point[] out and distinctly claim[]" in its claims "the subject matter which the inventor ... regards as the invention" and that the patent seeks to monopolize. 35 U.S.C. §112(b). That is the same "invention" that

§112(a) requires a patent to "enable any person skilled in the art ... to make and use." *Id.* §112(a). The result is straightforward: if the patent claims a broad genus as the "invention" under §112(b), then the patent must enable a skilled artisan to make and use that entire invention—the genus—under §112(a), not just whatever subset the patentee later asserts is really "needed" to "put the claimed inventive concept into practice." Br.29. The words "as needed" appear nowhere in §112, and nothing else in the text provides clues as to what and whose needs matter. This Court should reject Amgen's efforts to engraft language onto §112.

2. Without grounding in the statutory text, it is unsurprising that Amgen's only-as-needed standard finds no support in this Court's cases. Amgen begins with *Wood v. Underhill*, which pre-dates claiming practice and is distinguishable on that ground alone. 46 U.S. (5 How.) 1 (1847). The case is inapposite regardless. It involved a claimed "improvement in the art of manufacturing bricks" by mixing fine coal-dust with clay, and examined whether the patent was too vague to be valid because it only specified a "general rule" for the proportion of coal-dust to clay. 46 U.S. (5 How.) at 4-5. In answering that question, this Court deemed the specification sufficient, but not because it allowed a skilled artisan to practice the patent on some limited basis, by making whatever subset of bricks the Court believed was really "needed" to practice the invention. Instead, the Court made clear that the statutory standard was whether the patent allowed an artisan to make and use the patented invention "without making any experiments of his own," and underscored that if "no one could use the

invention without first ascertaining by experiment the exact proportion ... required to produce the result intended," then "undoubtedly it would be the duty of the court to declare the patent to be void." *Id.*

Mowry v. Whitney, which involved a process for manufacturing cast-iron railway wheels by cooling the entire wheel at the same rate, is to the same effect. 81 U.S. 620 (1871). As in *Wood*, this Court asked whether the patent disclosure was sufficient "to teach the public how to practice" the claimed invention, *id.* at 644, not just some limited subset. The Court found the disclosure adequate, not because it evaluated whether the disclosure "put the claimed inventive concept into practice" for particular railroad wheels on some "as needed" basis, Br.29, but because the disclosure enabled the entire "process invented and claimed," 81 U.S. at 645-46.

So too for *Minerals Separation, Ltd. v. Hyde*, 242 U.S. 261 (1916), which Amgen repeatedly invokes for the proposition that a patent's disclosure "'satisfies the law' so long as it 'sufficiently … guide[s] those skilled in the art to' the 'successful application' of 'the invention.'" Br.2; *see also* Br.6, 23, 24, 31-32, 41, 46. *Minerals Separation* is a remarkably thin reed for any enablement argument, as the decision principally addressed whether the patent was "invalid for want of novelty and invention." 242 U.S. at 263; *see id.* at 263-70. Only in a single paragraph did the Court address an alternative ground for invalidity, and without using the word "enablement" or referring to the statutory disclosure requirement; instead, the Court addressed the separate definiteness requirement, holding that the patent was "sufficiently definite." *Id.*

at 271; *see Nautilus*, 572 U.S. at 910 (describing *Minerals Separation* and its "not greater than is reasonable" statement as addressing definiteness, not enablement).

Regardless, there was no dispute in *Minerals Separation* that all "variation[s] of treatment" worked and were "within the scope of the claims"; experimentation (characterized as "preliminary tests") was required merely to determine the variables that "would be most successful and economical in each case" so as "to obtain the best results," not to make and use the full range of the invention claimed. 242 U.S. at 270-71. Thus, *Minerals Separation* not only fails to support Amgen's as-needed enablement requirement; it is fully consistent with the Court's (and the Federal Circuit's) unbroken line of decisions invalidating genus claims that require a skilled artisan to make and test candidates to find embodiments covered by the claims. *See, e.g.*, *Lamp*, 159 U.S. at 474-75; *Holland*, 277 U.S. at 256-57; *Idenix*, 941 F.3d at 1156-62.

3. Amgen's other cited authorities likewise do not support its as-needed standard. *See* Br.32-36. As already noted, British authorities invalidated patents for failing to enable the entire invention without undue experimentation. *See Arkwright*, Dav. Pat. Cas. at 106-17, Webs. Pat. Cas. at 67. Similarly, in *Neilson v. Harford*, 151 Eng. Rep. 1266 (Exch. 1841), the court did not apply an "as-needed" test, but asked instead whether the patent enabled the whole "machine for which a patent is taken out," without requiring the artisan to engage in further "invention or addition." *Id.* at 1274.

Amgen's early American authorities are to the same effect. In *Carver v. Braintree Manufacturing Co.*, Justice Story reviewed whether a patent adequately enabled an improved rib for the cotton gin by asking "[w]hether a skilful mechanic could from this description make a proper rib for *any particular kind of cotton*," 5 F.Cas. 235, 237 (C.C.D. Mass. 1843) (emphasis added)—not, as Amgen adds, "as needed." Br.34. Two of Amgen's cited treatises predate modern claiming practice but nonetheless confirm that the patent specification must enable the entire invention without experimentation. *See* W. Phillips, *The Law of Patents for Inventions* 283-84 (1837) (patent must enable skilled artisan "to make the machine ... without making any experiments, and without any new invention or addition of their own"); G. Curtis, *A Treatise on the Law of Patents for Useful Inventions* §156 (1849) ("to construct or reproduce the thing described, without invention or addition of their own, and without repeated experiments"). Professor Robinson's treatise—on which Amgen primarily relies—similarly explains that the patent must enable an artisan to practice the claimed invention "without experiment or the exercise of his own inventive skill." 2 W. Robinson, *The Law of Patents for Useful Inventions* §515 (1890).[6]

None of Amgen's pre-Federal Circuit decisions adopted an as-needed enablement standard, or examined how many embodiments are "practically"

[6] Professor Robinson was also distinctly opposed to purely functional claims like Amgen's, calling them "void" and "[o]ne of the most objectionable forms in which a claim can be stated." 2 Robinson §518.

needed to practice the invention; instead, they asked whether the patent adequately enabled the entire invention claimed (and invalidated patents that did not). *See, e.g.*, *Philip A. Hunt Co. v. Mallinckrodt Chem. Works*, 177 F.2d 583, 585-86 (2d Cir. 1949) (L. Hand, J.) (patent must enable "all practicable means, comprehended within the general language" of the claims, "without further substantial experimentation"); *see also Ill. Tool Works, Inc. v. Foster Grant Co., Inc.*, 547 F.2d 1300, 1309 (7th Cir. 1976) (enablement must be "commensurate in scope with the protection sought by the claims"); *In re Moore*, 439 F.2d 1232, 1235-36 (C.C.P.A. 1971) (enablement must be "commensurate with the scope of protection sought by the claims"); *In re Angstadt*, 537 F.2d 498, 501-02 (C.C.P.A. 1976) (same).

4. The PTO, unsurprisingly, follows the same approach. As its directions to patent examiners make clear, "[t]he focus of the examination inquiry is whether *everything within the scope of the claim is enabled*." *Manual of Patent Examining Procedure* §2164.08 (9th ed. 2020) (*MPEP*) (emphasis added). The PTO thus looks to whether skilled artisans "could readily determine *any one* of the claimed embodiments," *id.* (emphasis added)—not just whatever embodiments an examiner thinks might ultimately be needed in practice, which is entirely unknowable at the patent-issuance stage.

Amgen contends that the PTO instructs examiners that *Minerals Separation* "supplies the proper 'standard for determining whether the specification meets the enablement requirement.'" Br.42-43. But the enablement standard that the PTO

draws from *Minerals Separation* is not an "as needed" standard or any other standard proposed by Amgen; it is whether "the experimentation needed to practice the invention [is] undue or unreasonable," *MPEP* §2164.01, which is hardly unique to *Minerals Separation*. The PTO also instructs examiners that a skilled artisan must be able to "make and use the entire scope of the claimed invention without undue experimentation," *id.* §2164.08, and that a disclosure must be "commensurate with the scope of the claimed invention, *i.e.*, must reasonably enable the full scope of the claimed invention," *id.* §2164.05.

Finally, the irony of Amgen's insistence on an as-needed standard is that the specification here does not allow skilled artisans to make and use specific embodiments that they need or want to reproduce, or even any embodiment from entire classes of claimed antibodies. After all, a skilled artisan will not want or need to produce a random embodiment of the genus. Rather, skilled artisans (particularly after the patent expires and the patent bargain fully benefits the public) will want and need to produce particular undisclosed antibodies within the claimed genus that may be especially medically effective. For that very practical, as-needed task, Amgen's specification is next to useless.

Thus, while Amgen is correct that a patent is not enabled where skilled artisans (1) "cannot construct the claimed invention at all," (2) cannot "produce the invention without experimentation that exceeds what skilled artisans typically do," (3) cannot produce "a distinct category of embodiments," or (4) are left "searching for a needle in a haystack," Br.44-45, those

categories are hardly exhaustive. Another clear case of non-enablement is when skilled artisans cannot predictably produce specific undisclosed embodiments of the claimed invention (or even entire classes of undisclosed embodiments) that they want or need without engaging in a trial-and-error process that could take years. As the Federal Circuit correctly recognized, that scenario likewise demonstrates a failure to enable the full scope of an invention absent undue experimentation and defeats Amgen's patents.

III. Claims Like Amgen's Harm Innovation.

Amgen contends that the decision below invalidating its patents "has devastating consequences" by "threaten[ing] genus claims in any field whenever they cover more than disclosed examples." Br.39. Tellingly, however, the only wider impact Amgen identifies is a single, nonprecedential ruling by a PTO administrative panel that merely applied the *Wands* factors and concluded that "undue experimentation would be required to make and use the full scope of the claimed invention." *Ex Parte Beall*, 2021 WL 1208966, at *3 (P.T.A.B. Mar. 26, 2021). And that garden-variety determination invoked an enablement standard that Amgen does not challenge and did not turn on any "cumulative-effort" standard or "reach-the-full-scope" test.

Amgen argues that "[t]he impact on incentives to innovate is particularly severe in the biotech and pharmaceutical industries," specifically citing antibodies as at risk from the decision below. Br.39. But there are good reasons that many pharmaceutical and biotech firms that rely on patents and innovation disagree with Amgen. First, the Federal Circuit has

rejected enablement challenges to genus claims in the biotech or pharmaceutical industries when their full scopes are supported by the patent. *See, e.g.*, *Bayer Healthcare LLC v. Baxalta Inc.*, 989 F.3d 964, 970-71, 980-81 (Fed. Cir. 2021) (rejecting an enablement challenge to a genus claim to recombinant forms of human factor VIII because the patent provided instructions and examples that enabled the "full scope"); *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F.Supp.3d 629, 659-663 (E.D. Tex. 2017) (rejecting enablement challenge to a genus of PDE5 inhibitors to treat benign prostatic hyperplasia), *aff'd*, 739 F.App'x 643 (Fed. Cir. 2018). Second, in the two years since the decision below, companies have continued to innovate groundbreaking, lifesaving antibody treatments. *See* Peter Loftus, *FDA Authorizes Use of New Eli Lilly Covid-19 Antibody Treatment*, Wall St. J. (Feb. 11, 2022), https://on.wsj.com/3oZ3jtG. Even the academic article that Amgen espouses admits that, despite the Federal Circuit's supposed new enablement test making genus claims "nearly impossible," the biotechnology and pharmaceutical industries "seem to be doing just fine," and "innovation … seem[s] to be proceeding apace." Dmitry Karshtedt et al., *The Death of the Genus Claim*, 35 Harv. J.L. & Tech. 1, 64-65 (2021).

Amgen invokes the specter of "[c]opyists" who can "'avoid infringement' simply by making a 'minor change.'" Br.39. But this Court has a doctrine to address that risk. Under the doctrine of equivalents, "a product or process that does not literally infringe upon the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused

product or process and the claimed elements of the patented invention." *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997). Moreover, in this context, the science itself protects against the risk Amgen invokes, because making a few seemingly minor substitutions in the amino-acid sequence can radically change the blocking and binding characteristics of an antibody. *See, e.g.*, C.A.App.3768-69, 3891.

Finally, and most important, it is Amgen's invitation to allow companies to monopolize far more than they enable that poses the real risk to innovation in these fields. If an inventor purports to "invent[] a group of compositions defined by a genus but does not know enough to fully enable that genus," it "would suppress innovation if one were able to claim such a broad genus." Pet.App.65a.

This case perfectly illustrates the risks. In the first place, the chronology here belies any assertion that Amgen's genus claims spurred innovation. Amgen did not file its genus claims until years *after* multiple companies had independently pursued and discovered specific PCSK9-inhibiting antibodies, Amgen had obtained a patent on its Repatha antibody by structure, and Amgen had seen Sanofi/Regeneron's independently developed Praluent. *See* pp.6-10, *supra*.[7]

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[7] Amgen contends that Regeneron "used the 'anchor antibodies' disclosed in Amgen's applications to develop" Praluent. Br.15. But Regeneron filed its provisional patent application on Praluent two months *before* Amgen's patent application on Repatha published, and thus knew nothing about Amgen's

Moreover, allowing a company that has discovered only particular species to obtain a patent on a broad functionally claimed genus creates a very real risk that important medical treatments will never reach the market. Here, for example, Praluent and Repatha do not have the same FDA-approved indications or dosing; only Praluent is approved for a "low dose" therapy that guards against the possibility of too-low cholesterol. *See* D.Ct.Dkt.967, Ex.63, at 6 (Praluent label recommending that doctors start patients on low dose and noting that the "long-term effects of very low levels of LDL-C … are unknown"). Amgen's broad genus claim would force this low-dose option off the market, as Amgen literally tried to do via injunction earlier in this litigation.

But the even greater risk comes from the very real possibility that a company that lays claim to an entire functional and un-enabled genus will have only discovered species that are not medically efficacious at all. Pfizer's experience in developing a PCSK9 antibody is a cautionary tale. Pfizer was one of the first companies to begin development of a PCSK9 antibody, but after it discovered a promising species and filed a provisional patent application for that antibody by structure, it discontinued its program after disappointing clinical results, leading it to conclude that its antibody was "not likely to provide value to patients, physicians, or shareholders." *Pfizer Discontinues Global Development of Bococizumab, Its*

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independently-developed antibodies. *See* pp.8-9, *supra*. The Regeneron patent Amgen cites shows that Regeneron ran tests using publicly available antibodies (including Amgen's) only *after* having identified Praluent.

Investigational PCSK9 Inhibitor, Pfizer (Nov. 1, 2016), https://bit.ly/3wfLzh2. If Pfizer had instead laid claim to the entire genus, à la Amgen, it would have stifled innovation, and patients would have had no PCSK9 antibody therapies at all—or, at best, would have had to wait longer for Pfizer to develop a safe and effective antibody through trial and error.

IV. Amgen's Claims Are Not Enabled Under Any Viable Test For Enablement.

Amgen claims that "[u]nder any reasonable formulation of the statutory standard," its claims are enabled. Br.48. But very nearly the opposite is true: Under any reasonable formulation of the statutory standard, Amgen has not come close to satisfying it. Amgen does not actually take issue with the Federal Circuit law that pre-dated the decision below. And the district court, applying that law, had little difficulty in finding that Amgen had claimed far more than it enabled. The Federal Circuit unanimously reached the same conclusion. While Amgen tries to insert words—like "cumulative"—into the opinion and mischaracterize it in ways the panel expressly denied, the panel viewed this as a straightforward case under well-established law.[8]

The reason is simple: This is not a case where Amgen's specification leaves a skilled artisan just a few embodiments short of the invention's full scope. The specification here leaves a skilled artisan wholly

[8] Amgen's efforts to overclaim in this context have led to invalidation of its claims in the European Union. *See, e.g., European Patent Office Rules in Favor of Sanofi and Regeneron Concerning Praluent*, Sanofi (Oct. 29, 2020), https://bit.ly/3RmpZ4c.

unable to make and use any specific "needed" or desired antibody within the claimed genus beyond the handful of disclosed examples, including entire classes of claimed antibodies (like EGFa mimics or antibodies binding to more than nine of sixteen identified residues), or even to know whether antibodies produced using the disclosed techniques come within the genus absent further testing. Instead, the Amgen specification leaves skilled artisans seeking undisclosed embodiments exactly where they were before reading the specification: knowing from published research that certain undisclosed antibodies could be medically useful, and left to use well-known techniques to produce those potentially useful antibodies through trial and error. That is not a patent bargain at all, but a recipe for preempting useful research.

The undisputed evidence established that Amgen's specification fell far short of enabling the full scope of Amgen's claims under the *Wands* factors and other well-established and undisputed precedent. Both parties' witnesses agreed that (1) millions of antibodies could potentially fall within the claims' scope; (2) because even small changes to an antibody's amino acid sequence can change an antibody's functionality, a skilled artisan must test every generated antibody to determine whether it satisfies the claims' functional limitations; and (3) testing the antibody candidates generated from methods disclosed in the patent would be such an enormous undertaking that no scientist would even fathom doing it. *See* pp.13-15, *supra*; C.A.App.3902, 3914. The patents merely recite an iterative trial-and-error process and no more enable the full scope of the

functional claims than the patents held non-enabled in this Court's decisions in *Lamp*, *Holland*, *Béné*, and *Corona* and the Federal Circuit's decisions in *Idenix*, *Enzo*, and *Wyeth*—the last three of which the Federal Circuit applied in concluding non-enablement here and Amgen does not challenge.

Amgen repeatedly points to evidence that, "by following the patents' roadmap," skilled persons "can generate other claimed antibodies *every time*," and "'would be *certain* to make *all*' the antibodies across the claims." Br.49; *see also* Br.3, 17, 25, 48. But the so-called "roadmap" is nothing more than standard techniques for generating additional candidate antibodies that would still need to be tested, accompanied by disclosure of two dozen of the millions of species potentially within the genus. Indeed, it is telling that Amgen's disclosed exemplars have little in common with the most promising antibodies independently developed by other companies using the same well-established techniques, as the chart above well illustrates. *See* p.15, *supra*.

The fact that the "roadmap" allows skilled artisans to generate some antibodies that fall somewhere in the vast functionally-defined genus does not enable them to do anything they could not already do (and were already doing at at least three other companies). Furthermore, Amgen's patents unquestionably do not teach skilled artisans how to produce a *particular* needed but undisclosed antibody within the claims' scope, let alone how to do so without undue experimentation. No skilled person could take Amgen's patents and produce Praluent absent extraordinary experimentation. Indeed, Amgen's own

documents showed that despite having the '165 and '741 patents in hand, Amgen itself—the so-called innovator armed with the specification *and* all its other knowledge—could not make a single antibody in an entire class of antibodies (EGFa mimics) known to fall within the claims' scope that its competitors had produced. *See* C.A.App.9674-75, 9703-10, 9714-15, 9529, 9690, 9694-97, 9722-23. In other words, despite claiming a genus as its invention, Amgen itself could not make entire categories of species within that genus. That is the antithesis of enabling the "invention." 35 U.S.C. §112(a).[9]

Amgen repeatedly asserts that nobody "identified *any* actual antibody that required undue experimentation to make under the patents' teachings." Br.49; *see also* Br.3, 19, 25. Not so. Praluent and the Pfizer and Merck antibodies are such antibodies, as is *any* antibody that binds to more than nine residues—the maximum number to which Amgen's disclosed examples bind—even though the claimed genus includes antibodies that bind to up to sixteen residues. Pet.App.13a n.1. Such an antibody would be a coveted discovery, but Amgen's patent does not remotely enable it despite claiming it for Amgen's own. Claiming up to sixteen while enabling only up to nine is no minor overreach. Regardless, Amgen's

[9] According to Amgen, its expert testified that "the patents' roadmap produces" Praluent and other competitor antibodies. Br.50-51. But even Amgen's lead inventor admitted the patents do not disclose antibodies binding to more than nine claimed residues, D.Ct.Dkt.864 at Tr.535-37, and Praluent binds to 13, *see* p.15, *supra*. Regardless, the testimony Amgen cites is conclusory and does not account for the undue experimentation necessary to "produce[]" those specific antibodies.

argument only underscores the problem with its specification, which gives skilled artisans no way even to *identify* (let alone make and use) the full breadth of the claimed genus—making it impossible to identify more "actual" antibodies that require undue experimentation without doing that experimentation first. Nothing in law or logic requires a patent challenger actually to engage in undue experimentation just to prove that undue experimentation is required.

Amgen contends that Sanofi/Regeneron "identified not one conservative substitution to a claimed antibody that destroyed its activity." Br.50. But that is irrelevant when, as Amgen's own witnesses conceded, even "conservative" substitutions can result in changed functionality, thus requiring testing. C.A.App.3768-3769. Amgen mischaracterizes testimony by a Sanofi/Regeneron expert that such "minor variants" are "essentially copies of each other," Br.50; that expert was comparing certain disclosed antibodies that were nearly identical in structure and were assumed for purposes of the expert's testimony to fall within the claims. C.A.App.3787-88. Moreover, even if conservative substitutions could predictably generate new undisclosed embodiments, they would enable only antibodies similar to those few whose sequences Amgen disclosed—a far cry from enabling the claimed genus. Amgen did not content itself with claiming a genus limited by structure, but rather claimed an entire functional genus with no shared unique structural features and supplied a specification that gave skilled artisans no meaningful guidance to find any particular undisclosed species within that genus.

Amgen states in passing that "the Federal Circuit repeatedly decided factual issues contrary to the jury's presumed findings." Br.51. It cites only its prior briefing for this proposition, however, and this Court should not consider that undeveloped and highly factbound argument. *See South Dakota v. Bourland*, 508 U.S. 679, 697 (1993). Regardless, the Federal Circuit consistently relied on the *undisputed* evidence to affirm the district court's ruling that Amgen's patents were not enabled as a matter of law. *See, e.g.*, Pet.App.13a (discussing what "[o]ne of Amgen's expert witnesses admitted" and "[a]nother of Amgen's experts conceded").

In the end, Amgen is correct about only one thing: this case "does not require a third trip through the Federal Circuit." Br.51. Amgen's good-for-one-case-only arguments targeting statements ranging from non-existent to fleeting in the decision below provide no reason for disturbing the judgment of invalidity reached by the two courts below applying text and well-established and undisputed precedents like *Wands*, *Idenix*, and *Wyeth*. The chasm between what Amgen claimed and what it enabled is not measured in microns and does not turn on some subtle innovation in the decision below. The text of §112 and a host of this Court's precedents require the specification to enable the full scope of the invention, not leave skilled artisans where they started with no ability to make and use particular claimed antibodies with anything but trial and error using well-established techniques. The courts below were correct to invalidate Amgen's effort to monopolize what it has not enabled.

CONCLUSION

This Court should affirm.

Respectfully submitted,

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