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 PETITIONERS


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## QUESTION PRESENTED

Section 112 of the Patent Act provides that a patent's "specification shall contain a written description of the invention, and of the manner and process of making and using it," sufficient "to enable any person skilled in the art * * * to make and use the" invention. 35 U.S.C. § 112(a). The requirement that the specification teach skilled artisans "to make and use" the invention is referred to as the "'enablement'" requirement. *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 379 (1996). The question presented is:

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 BELOW AND CORPORATE DISCLOSURE STATEMENT

Petitioners Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc. were plaintiffs in the district court and appellants in the court of appeals. Respondents Sanofi, Aventisub LLC, f/k/a Aventis Pharmaceuticals Inc., Regeneron Pharmaceuticals, Inc., and Sanofi-Aventis U.S. LLC were defendants in the district court and appellees in the court of appeals.

Pursuant to this Court's Rule 29.6, petitioners state that the corporate disclosure statement in the petition for a writ of certiorari remains accurate.

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## BRIEF FOR PETITIONERS

## INTRODUCTION

The Federal Circuit "once again" has "impose[d] limitations on the Patent Act that are inconsistent with the Act's text." *Bilski* v. *Kappos*, 561 U.S. 593, 612 (2010). The Act requires that patents 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) (emphasis added). Virtually unchanged from the Patent Act of 1790, that command—the "enablement" requirement—embodies the Patent Act's "bargain": In exchange for a limited-time, exclusive right to their inventions, inventors

must publicly disclose their inventions, as well as how to make and use them, so the public may practice the inventions once the period of exclusivity expires. *Pfaff* v. *Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998).

For over a century, this Court has read the enablement requirement to mean what it says: A patent "satisfies the law" so long as it "sufficiently * * * guide[s] those skilled in the art to" the "successful application" of "the invention." *Minerals Separation, Ltd.* v. *Hyde*, 242 U.S. 261, 271 (1916). The statute's demands are "not greater than is reasonable, having regard to [the patent's] subject matter." *Id.* at 270.

Departing from statutory text, precedent, and history, the decision below announces a different standard—one that fundamentally alters the patent bargain. It is no longer sufficient that the patent enable skilled artisans to "make and use" the invention. Instead, skilled artisans must be able to "*reach the full scope* of claimed embodiments"—*i.e.*, to cumulatively identify and make all, or nearly all, possible variations of the invention—without "'substantial time and effort.'" Pet. App. 14a (emphasis added). That standard, the panel acknowledged, "raises the bar," imposing "high hurdles in fulfilling the enablement requirement." Pet. App. 12a-13a.

The Patent Act nowhere imposes that standard. There may be myriad variations on James Watt's steam engine or the Wright Brothers' airplane. But the law has never required that, for those inventions to be patentable, skilled artisans must be able to cumulatively identify and make every *variation* without substantial time and effort. The folly of a "make all embodiments" requirement has been recognized by learned commentators from the 19th century, see 2 W. Robinson, *The Law of Patents for Useful Inventions* § 486 (1890), through present day, see D. Kar-

shtedt *et al.*, *The Death of the Genus Claim*, 35 Harv. J.L. & Tech. 1 (2021) ("Karshtedt"). It would render unpatentable *any* invention that covers a "nontrivial" number of variations. *Id.* at 4. This Court long ago recognized that it is "not necessary to * * * describe in the specification[ ] all possible forms in which the claimed principle may be reduced to practice." *Smith* v. *Snow*, 294 U.S. 1, 11 (1935).

If the patent teaches skilled artisans how to "make and use" the invention as needed, the *cumulative* time and effort it would take to make each and every variation should be irrelevant. The Federal Circuit's concern that patentees might attempt to monopolize more than they invented through overly broad claims, Pet. App. 12a-13a, was answered long ago in *Consolidated Electric Light Co.* v. *McKeesport Light Co.*, 159 U.S. 465 (1895), which applied the statutory standard to invalidate claims where there was proof that the patent's instructions were not enabling for large classes of claimed subject matter.

There was no such evidence here. Amgen's invention—monoclonal antibodies that dramatically reduce "bad" cholesterol—was a breakthrough. There was no dispute Amgen's patents enable skilled artisans to "make and use" those antibodies. 35 U.S.C. § 112(a). At trial, Amgen presented evidence that following the patents' roadmap produces claimed antibodies *every time*, and that the roadmap could produce *all* antibodies within the claims. No one—not respondents, not the courts below—identified even *one* actual antibody that could *not* be produced using the patents' disclosures.

The jury thus found for Amgen on enablement. Overturning that verdict, the Federal Circuit speculated that there *might* be "millions of candidates" that fall within the claims, each of which would have to be "generate[d] and then screen[ed]" to determine whether it met the claims'

requirements. Pet. App. 15a. It theorized there *might* be undisclosed antibodies at the "far corners of the claimed landscape that were particularly inaccessible or uncertain." Pet. App. 65a. Consequently, the court ruled, "'substantial time and effort' would be required *to reach* the full scope of claimed embodiments." Pet. App. 14a (emphasis added).

The statutory standard and this Court's cases, however, look to whether skilled artisans can "make and use" the invention. To prove patent claims are not enabled, challengers must demonstrate—by clear-and-convincing proof—that skilled artisans cannot practice the invention by following the patent's teachings or that doing so would require undue experimentation. Speculation that there might be some unknown embodiment out there that might require time and effort to find does not suffice. Respondents argued that various antibodies covered by Amgen's patents could not be made by following the patents' instructions, but the jury rejected those arguments given Amgen's evidence that the patents' roadmap would produce those antibodies. Amgen's patents satisfy the statutory standard for enablement. The Federal Circuit's contrary ruling under a reach-the-full-scope test cannot stand.

## OPINIONS BELOW

The court of appeals' opinion (Pet. App. 1a-15a) is reported at 987 F.3d 1080; its opinion denying rehearing (Pet. App. 58a-68a) is published at 850 F. App'x 794. The district court's opinion (Pet. App. 16a-54a) is unreported.

## STATEMENT OF JURISDICTION

The Federal Circuit entered judgment on February 11, 2021 (Pet. App. 1a-15a), and denied rehearing on June 21, 2021 (Pet. App. 58a-68a). By general order, this Court ex-

tended the time to file the petition to November 18, 2021. Petitioners filed the petition on that date, and the Court granted the petition on November 4, 2022. This Court has jurisdiction under 28 U.S.C. § 1254(1).

## STATUTORY PROVISION INVOLVED

The relevant provision of the Patent Act, 35 U.S.C. § 112(a), is set forth in the petition appendix (Pet. App. 69a).

## STATEMENT

This case concerns whether the Patent Act's "enablement" requirement is governed by the statutory standard, which requires patents to teach skilled artisans to "make and use" the claimed invention, 35 U.S.C. § 112(a), or whether patents instead must enable skilled artisans "*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).

### I. STATUTORY FRAMEWORK

This Nation's patent laws reflect "a carefully crafted bargain." *Pfaff*, 525 U.S. at 63. In exchange for publicly disclosing their inventions, as well as how to make and use them, inventors receive the exclusive right to their inventions for a limited time. *Ibid.* That is patent law's "*quid pro quo*." *Universal Oil Prods. Co.* v. *Globe Oil & Refin. Co.*, 322 U.S. 471, 484 (1944).

Section 112 of the Patent Act sets forth the inventor's side of the bargain: Patents must "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*." 35 U.S.C. § 112(a) (emphasis added). That is known as the

"'enablement'" requirement. *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 379 (1996).[1] "The object" of §112 "is to require the patentee to describe his invention so that others may construct and use it after the expiration of the patent." *Schriber-Schroth Co.* v. *Cleveland Tr. Co.*, 305 U.S. 47, 57 (1938).

The enablement requirement was inherited from Framing-era English patent practice "in which juries were asked to determine whether the specification described the invention well enough to allow members of the appropriate trade to reproduce it." *Markman*, 517 U.S. at 379. The requirement was codified by the original Patent Act of 1790, in language strikingly similar to that found in today's §112: The patent must include a "specification in writing, containing a description * * * so particular" as to "enable a workman or other person skilled in the art or manufacture * * * to make, construct, or use" the invention. Act of Apr. 10, 1790, ch. 7, §2, 1 Stat. 109, 110-111. Throughout the Patent Act's iterations, the enablement requirement has remained largely unchanged. See Act of Feb. 21, 1793, ch. 11, §3, 1 Stat. 318, 321-322; Act of July 4, 1836, ch. 357, §6, 5 Stat. 117, 119; Act of July 8, 1870, ch. 230, §26, 16 Stat. 198, 201; see also P.J. Federico, *Commentary on the New Patent Act* (West 1954), reprinted in 75 J. Pat. & Trademark Off. Soc'y 161, 185-186 (1993).

Consistent with statutory text, this Court has explained that a patent's disclosure "satisfies the law" if it is "sufficiently definite to guide those skilled in the art to" the "successful application" of "the invention," *Minerals Separation*, 242 U.S. at 271; if it teaches skilled artisans "to

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[1] The Federal Circuit has construed §112(a) as containing two legal requirements: "enablement" and "written description." *Ariad Pharms., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (en banc).

practice the invention," *Universal Oil*, 322 U.S. at 484; or if it "points out some practicable way of putting [the invention] into operation," *The Telephone Cases*, 126 U.S. 1, 536 (1888).

## II. PROCEEDINGS BELOW

### A. Amgen Invents and Patents Antibodies that Dramatically Lower Cholesterol

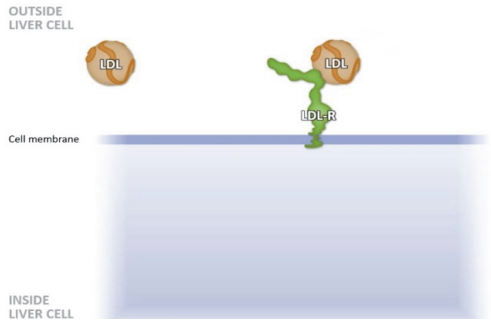
High LDL cholesterol causes heart disease, the leading cause of death in the United States. C.A. App. 3793 (487:24-488:4). For many patients, traditional medicines, like statins, are insufficient. *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1371 (Fed. Cir. 2017).

This case concerns Amgen's breakthrough invention—a class of monoclonal *antibodies* that *lower LDL cholesterol levels*. Those antibodies bind at a precise location on a protein called "PCSK9" and, in doing so, block PCSK9 from impairing the body's mechanisms for removing cholesterol. U.S. Patent No. 8,829,165, C.A. App. 37-420; and No. 8,859,741, C.A. App. 421-806. Amgen invested billions of dollars and a decade of research bringing that invention to market. C.A. App. 3793 (488:8-12).

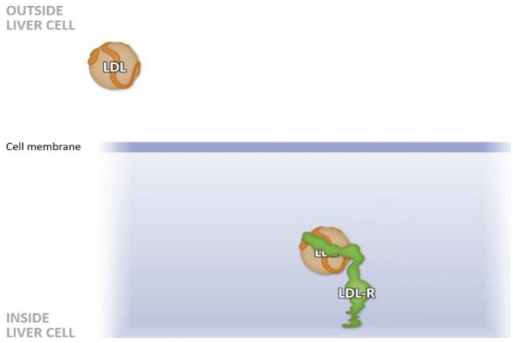
#### 1. *Amgen Invents a Class of Antibodies that Bind PCSK9's "Sweet Spot" and Block Its Interaction with LDL Receptors*

Amgen's efforts began in 2005, when Dr. Simon Jackson studied a protein called PCSK9. C.A. App. 3795 (493:21-495:13). PCSK9 exists naturally in the human body. At the time, PCSK9 was thought to affect LDL cholesterol levels, but no one understood how. *Ibid.*

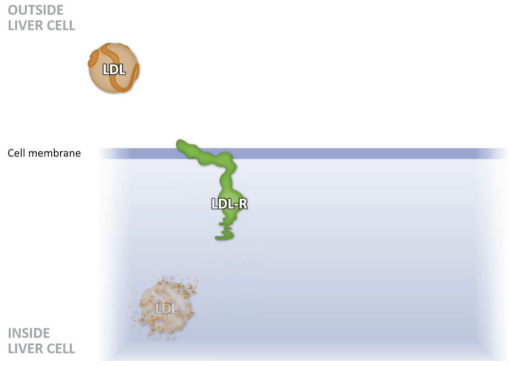
Ordinarily, the body removes LDL cholesterol from the bloodstream using LDL receptors on the surface of liver cells. Pet. App. 3a. The receptors "bind" to LDL cholesterol to capture it.




C.A. App. 9992. The cholesterol-receptor complex is then internalized into the cell.

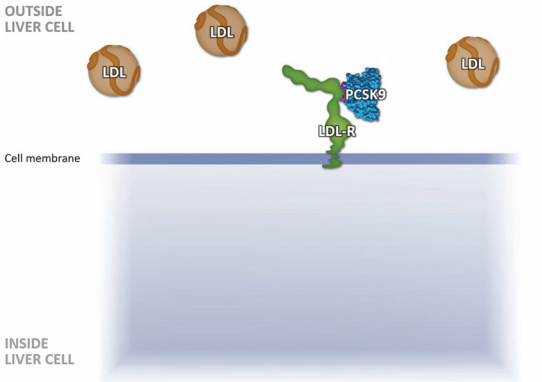



*Ibid.* Finally, the cholesterol is destroyed inside the cell and the receptor recycles to the surface to capture more cholesterol.

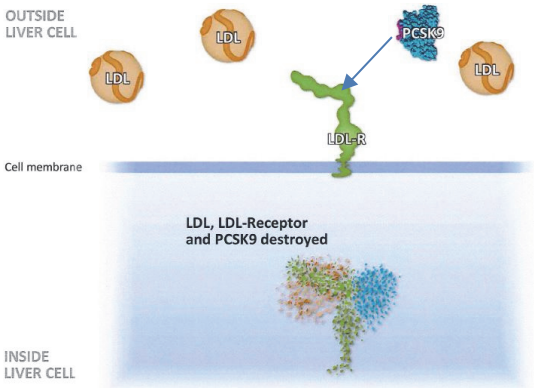



*Ibid.*; C.A. App. 3796 (499:10-18).

Dr. Jackson discovered that *PCSK9* binds "directly" to "LDL receptor[s]." C.A. App. 3795 (494:19-495:13).



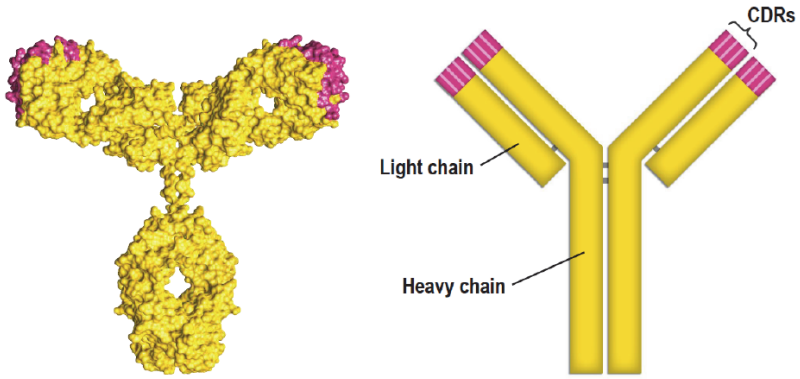

When PCSK9 binds to LDL receptors, PCSK9 *and the receptors* are destroyed inside the cell.




C.A. App. 4040, 3679 (181:23-182:20). The reduction of LDL receptors available to remove LDL causes LDL levels to rise. C.A. App. 3679 (181:23-182:20).

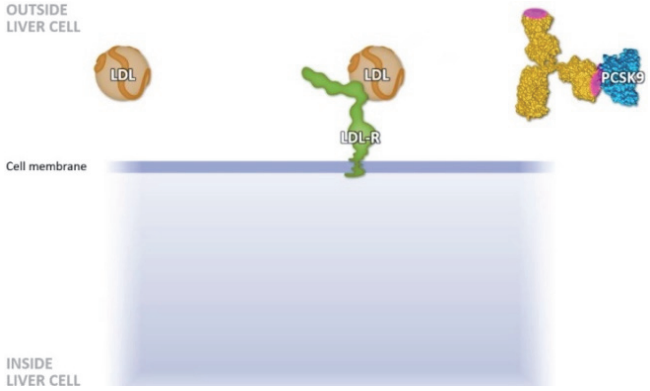
Dr. Jackson posited he could create *antibodies* to combat PCSK9's destructive effect on LDL receptors. Anti-

bodies are proteins composed of amino-acid chains; they typically are produced in response to antigens, like bacteria or viruses, the body recognizes as foreign.



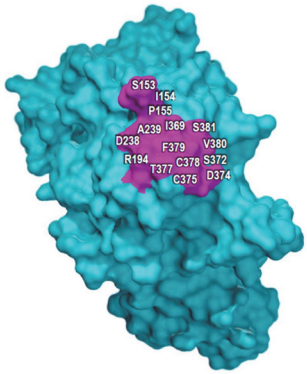

C.A. App. 4134.

Dr. Jackson created monoclonal antibodies that, due to their structural and chemical properties, "bind to PCSK9 in the special region"—or "sweet spot"—where PCSK9 would otherwise bind LDL receptors. C.A. App. 3796 (498:16-499:2), 3799 (509:9-510:3). By binding there, the antibodies *block* PCSK9 from binding to LDL receptors. *Ibid.*




C.A. App. 9993.

PCSK9's sweet spot—purple in the graphic below—comprises only 15 of PCSK9's 692 amino acids. C.A. App. 3802 (524:10-11), 3900 (724:15-16), 247 (100:5-10).




C.A. App. 4152. It has a "unique" three-dimensional structure and "distinct" "chemical characteristics." C.A. App. 3880 (644:4-10). Only a limited number of antibody structures can fit its "topology." C.A. App. 3880 (644:4-10), 3901-3902 (730:21-731:3).

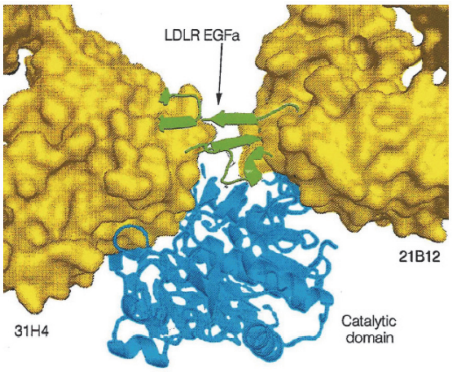
Dr. Jackson's team designed protocols, using super-immunized mice, to generate and select antibodies with the shape and chemical complementarity to bind PCSK9's sweet spot—and thereby block PCSK9 from binding LDL receptors. C.A. App. 3876 (628:12-629:21); Pet. C.A. Br. 5-9, 13-16.

2. *Amgen's Patents Disclose PCSK9 Antibodies and Detailed Instructions that Teach Artisans How To Make Them*

The U.S. Patent and Trademark Office issued the '165 and '741 patents with claims to monoclonal antibodies that bind one (or more) of the amino acids in PCSK9's sweet spot, and thereby block PCSK9 from binding to LDL receptors. Pet. App. 3a; C.A. App. 411-412, 796-797. Am-

gen's patents are a "rich handbook," providing "a wealth of information" about the claimed antibodies. C.A. App. 3910 (763:1-12).

Example antibody sequences. The patents disclose 26 example antibodies, characterized by amino-acid sequence, that bind PCSK9's sweet spot and thereby block PCSK9 from binding to LDL receptors. C.A. App. 51-116 (Figs. 2A-3JJJ), 240 (85:9-43). The patents also disclose the results of Amgen's x-ray crystallography studies on two antibodies—21B12 and 31H4—providing an atomic-level picture of where those antibodies bind to PCSK9. C.A. App. 169-171 (Figs. 19A-19B, 20A), 174-176 (Figs. 20D-20F), 247-249 (Exs. 28-31). Those two antibodies bind across the sweet spot—one on each side—precisely where LDL receptors would bind if an antibody did not already occupy the binding site. C.A. App. 3876 (630:19-25).




C.A. App. 171 (Fig. 20A). Consequently, as explained below, skilled artisans can use 21B12 and 31H4 as "anchor" antibodies to identify any other antibodies that bind anywhere on PCSK9's sweet spot. C.A. App. 3904 (742:6-13). Antibody 21B12 is the basis for Amgen's Repatha®, the first PCSK9 inhibitor approved worldwide to treat high

LDL cholesterol. C.A. App. 3793 (488:18-24), 3800 (513:23-514:2).

Instructions for generating additional antibodies. The patents' specification sets out a step-by-step "roadmap" for generating antibodies, beyond the 26 examples, that fall within the patents' claims. See Pet. C.A. Br. 13-16. Amgen, the patents disclose, had isolated many more antibodies that bind the sweet spot and block PCSK9's interaction with LDL receptors: By immunizing two panels of 10 mice each, Amgen had identified 384 antibodies that block PCSK9 from binding LDL receptors "well," 85 of which block the interaction by "greater than 90%." C.A. App. 234 (Tbl. 3), 236-237 (77:66-80:37), 3797-3798 (504:4-506:25).

The roadmap leverages the inventors' anchor antibodies—21B12 and 31H4—as a shortcut to obtain the other antibodies that bind PCSK9's sweet spot and thereby block it from binding to LDL receptors. C.A. App. 3904 (742:6-13). The roadmap describes in detail how to use those anchor antibodies with "methods for obtaining and screening monoclonal antibodies" that had been "well known" in the art for decades. *In re Wands*, 858 F.2d 731, 736 (Fed. Cir. 1988).

*First*, the patents instruct skilled artisans to make either antibody 21B12 or 31H4 using the amino-acid sequences the patents provide. C.A. App. 238-239 (Exs. 4.1-5), 59 (Fig. 3E), 90 (Fig. 3JJ), 3903 (737:12-738:10).

*Second*, the patents direct scientists to inject PCSK9 into mice to generate antibodies that bind to PCSK9. Pet. App. 38a-39a.[2] The "extensive schedule" of immuniza-

[2] The patents teach that, alternatively, phage display—a non-animal means of generating antibodies, C.A. App. 3896 (709:2-10)—can be

tions disclosed in Amgen's patents maximizes their production of the "full spectrum" of PCSK9 antibodies. C.A. App. 3904 (739:21-740:11), 3797 (501:2-502:15), 234 (Tbl. 3). The patents explain how to use Amgen's enhanced assays to identify the mouse-produced antibodies that bind somewhere on PCSK9. See C.A. App. 236-238 (Ex. 3). The assays screen hundreds of antibodies at once. C.A. App. 3797 (503:18-504:18), 3898 (718:3-23).

*Third*, the patents teach using one of the "anchor" antibodies from step one—21B12 or 31H4—in competition assays to identify the antibodies from step two that bind to PCSK9's sweet spot. C.A. App. 3904 (741:24-742:13). If a generated antibody binds at the part of the sweet spot covered by an anchor antibody, they will "compete," as they cannot both occupy the same spot. That gives artisans "a very good idea" that the new antibody binds to the "sweet spot" and falls within the claims. *Ibid.* Those competition assays are also high-throughput. See C.A. App. 241 (88:34-47), 3909 (761:1-762:1).

*Fourth*, the patents teach running Amgen's optimized blocking test to confirm that the antibodies from step three—those that compete with 21B12 or 31H4—block PCSK9's interaction with LDL receptors. C.A. App. 3904-3905 (742:14-743:17), 3798 (505:2-8). The patents also explain that skilled artisans can perform alanine scanning to "verif[y] * * * exactly which amino acids" on PCSK9 the "antibodies are binding to." C.A. App. 3905 (744:20-745:12); see C.A. App. 244 (Ex. 18).

Conservative substitution. The patents also describe how artisans, with a claimed antibody in hand, can make "variants" using another "well-known technique[ ]" called

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used, C.A. App. 223 (52:23-42), 225 (55:1-5); see C.A. App. 3909 (759:7-17).

"conservative amino acid substitution[ ]." C.A. App. 221 (48:21-23, 48:29-33), 3917 (792:23-793:3); see Pet. C.A. Br. 17. Conservative substitution involves replacing selected amino acids in the antibody with others known to have "common * * * properties." C.A. App. 211 (27:32-39, 28:1-5, Tbl. 1). The variants are expected to "retain a similar biological activity" as the original. C.A. App. 211 (27:60-62). Variants made through conservative substitutions with one or two changes are over 99% similar to the original antibody—"essentially copies." C.A. App. 3788 (467:7-15); see Pet. C.A. Br. 17 & nn.5-6. "Conservative" substitutions thus are made without "substantially chang[ing] the structural characteristics of the parent sequence," C.A. App. 222 (49:65-50:1), and "without destroying" antibody "activity," C.A. App. 221 (48:23-33).

**B. Two Juries Find Amgen's Patents Valid**

1. After Amgen filed its first patent application in 2007, C.A. App. 3800 (514:3-18), Regeneron used the "anchor antibodies" disclosed in Amgen's applications to develop the PCSK9 antibody alirocumab (marketed as "Praluent"). Having screened mouse-generated antibodies, Regeneron tested its lead antibodies against Amgen's anchor antibodies 21B12 and 31H4. See U.S. Patent No. 8,357,371 ("'371 patent"). Those tests showed that Praluent (laboratory name 316P) competes with both Amgen anchor antibodies and thus binds to PCSK9's sweet spot. *Id.* at 34:25-34, Tbl. 22.[3]

2. In October 2014, Amgen sued respondents Sanofi and Regeneron ("Sanofi-Regeneron") for patent infringe-

[3] "Control II" in Table 22 of Regeneron's patent is Amgen's anchor antibody 31H4. See '371 patent, at 26:39-40; C.A. App. 59. "Control III" in Table 22 is Amgen's anchor antibody 21B12. See '371 patent, at 28:3-4; C.A. App. 90.

ment, alleging that Praluent infringes Amgen's '165 and '741 patents. Pet. App. 5a. One month after Amgen filed suit, Sanofi-Regeneron purchased a priority-review voucher so Praluent would leapfrog Amgen's Repatha in the FDA review queue. D. Ct. Dkt. 864 at 488:18-490:1; see 21 U.S.C. § 360ff. Consequently, although Amgen sought FDA approval three months before Sanofi-Regeneron, the FDA approved Sanofi-Regeneron's Praluent one month before approving Amgen's Repatha. *Amgen*, 872 F.3d at 1371-1372.

3. Sanofi-Regeneron stipulated to infringement, see *Amgen*, 872 F.3d at 1372, but asserted multiple invalidity defenses, including lack of "written description" and "enablement," Pet. App. 5a. Two juries found Amgen's patents valid. Pet. App. 5a-6a.

After the first trial, the jury rejected Sanofi-Regeneron's invalidity challenges, and the district court denied JMOL. C.A. App. 2061-2065, 2885. The Federal Circuit vacated and remanded for a new trial. See *Amgen*, 872 F.3d at 1375-1382. The court ruled that Sanofi-Regeneron, to support its non-enablement argument, should have been permitted to present evidence of PCSK9 antibodies developed after Amgen's patents were filed. *Id.* at 1375.

4. After a second trial, another jury rejected Sanofi-Regeneron's validity challenges. Pet. App. 6a. The district court upheld the jury's verdict that the patents provided an adequate written description. Pet. App. 23a-27a. While the court acknowledged "conflicting testimony" on many issues, *e.g.*, Pet. App. 35a, it overturned the jury's enablement verdict as a matter of law, Pet. App. 31a-44a, holding that "undue experimentation would be needed to practice the" claims' "full scope," Pet. App. 44a.

The court did not identify an actual antibody within the claims that the patents failed to enable. Instead, it cited Sanofi-Regeneron's speculation that "'you *could be* immunizing mice for a hundred years,'" but "'[t]here *might be kind of* an antibody that you didn't come up with in that time period.'" Pet. App. 42a (emphasis added). The court also invoked "conservative substitution" to suggest that many potential variants of working antibodies could be generated and tested. Pet. App. 43a-44a. It did not dispute, however, that Sanofi-Regeneron never identified *any* conservative substitution that destroyed the activity of any claimed antibody.

### C. Proceedings Before the Federal Circuit

The Federal Circuit affirmed. Pet. App. 1a-15a.

1. On appeal, Sanofi-Regeneron again failed to identify a *single* antibody within the claims that would not be generated quickly and easily by following the patents' teachings. Pet. C.A. Br. 37-38. No one disputed that the jury heard testimony that Amgen's roadmap will "generate" antibodies within the claims every time, C.A. App. 3908 (756:8-20, 757:12-14), 3909 (762:14-20), or that skilled artisans following the patents' roadmap "would be *certain* to make *all* of the claim's antibodies," C.A. App. 3909 (762:10-20) (emphasis added); see C.A. App. 3908-3909 (757:12-760:21), 3918-3919 (798:25-799:5). Sanofi-Regeneron never identified even *one* variant made with conservative substitution that failed to work. Pet. C.A. Br. 59; Pet. C.A. Reply 14-15. While Sanofi-Regeneron had obtained a new trial to present antibodies that supposedly were not enabled—arguing that four were not—it never argued on appeal that the jury was required to find Sanofi-Regeneron had proved one or more of those not enabled. Pet. C.A. Reply 3.

The Federal Circuit nonetheless held Amgen's claims not enabled. Pet. App. 15a. Proving a claim "invalid for lack of enablement," the court observed, requires "clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without undue experimentation." Pet. App. 7a (quotation marks omitted). But it held that genus claims like Amgen's confront uniquely "high hurdles in fulfilling the enablement requirement." Pet. App. 12a. Genus claims "cover[ ] a group of structurally related products that incorporate the basic advance of the patented invention." Karshtedt, at 3. They often recite structural elements or formulas in combination with functional language (the desired action or result) to cover the "embodiments of the invention" sharing the common inventive feature. *Id.* at 13.

For genus claims with "functional claim limitations," the Federal Circuit held, "'undue experimentation can include'" the effort to "'identify[ ]'" all potential variations of the invention that meet the claim's requirements. Pet. App. 12a. The Federal Circuit asks how much experimentation "would be required" for skilled artisans "*to reach the full scope* of claimed embodiments," Pet. App. 14a (emphasis added)—*i.e.*, the cumulative effort necessary to identify and make all, or nearly all, variations of the invention that might exist within the genus. If doing so would require "'substantial time and effort,'" the patent is not enabled—even if individual embodiments across the invention can be made easily. *Ibid.*

The Federal Circuit acknowledged that "[t]he parties dispute[d]" myriad factual issues at trial. Pet. App. 12a. But it ruled that the claims were not enabled because, "to reach the full scope of claimed embodiments," Pet. App. 14a, skilled artisans would have "to first generate and then

screen" every theoretical "candidate" "to determine whether it" falls within the claims, Pet. App. 15a. The Federal Circuit posited that "millions of candidate[ ]" antibodies might need testing; that the antibody arts are "unpredictable"; and that the patents lack "adequate guidance" beyond the 26 "working examples." Pet. App. 13a-15a; contra C.A. App. 3883 (658:1-5). The Federal Circuit did not dispute that making individual embodiments was easy. Yet it held the claims were not enabled because "reach-[ing] the full scope of claimed embodiments" would require "'substantial time and effort.'" Pet. App. 15a.

2. The Federal Circuit denied rehearing. In an opinion respecting denial, Pet. App. 58a-68a, the panel addressed "[a]mici and others bemoaning" the panel's reach-the-full-scope test, Pet. App. 63a. The "limited guidance in the specification," it insisted, "made *far corners of the claimed landscape* * * * particularly inaccessible or uncertain." Pet. App. 65a (emphasis added). The opinion, however, did not identify any actual embodiment skilled artisans would consider "inaccessible or uncertain."

## SUMMARY OF ARGUMENT

I. A. Section 112 of the Patent Act requires that patents provide a description "of the invention, and of the manner and process of making and using it," that is sufficient to "enable any person skilled in the art * * * to make and use the same." 35 U.S.C. § 112(a). For two centuries, this Court and others have described and applied the enablement standard consistent with that text. The Federal Circuit's decision below, however, imposes a different standard for certain patent claims, requiring that skilled artisans be able to "*reach the full scope* of claimed embodiments"—*i.e.*, to cumulatively identify and make all, or nearly all, possible variations of the invention—without "'substantial time and effort.'" The Federal Circuit ack-

nowledges that standard "raises the bar" for enablement. The Federal Circuit's new standard has no basis in § 112's text.

B-C. Centuries of precedent refute the Federal Circuit's reach-the-full-scope test. This Court has never suggested that enablement turns on the cumulative "'time and effort'" that would be required to make all, or virtually all, of a claimed invention's potentially numerous embodiments. It has repeatedly upheld patents that would have flunked such a test. Enablement decisions from Framing-era English courts, early American circuit courts, and the regional courts of appeals before the Federal Circuit's creation all defy that new standard. The fact that no court had identified a reach-the-full-scope test in those many years confirms the Federal Circuit's error.

D. The Federal Circuit's reach-the-full-scope standard serves no valid patent-law policy and harms innovation. The Federal Circuit's test fundamentally alters the basic patent bargain, denying an inventor a patent based sheerly on the number of possible embodiments, even if the patent's disclosures teach the world how to "make and use" the claimed invention. The Federal Circuit's test discourages breakthrough innovations by cutting off patent protection for the most significant inventions simply because they have *too many* useful applications. That threatens devastating consequences.

II. A. Section 112 itself supplies the controlling standard: The specification must "enable any person skilled in the art * * * to make and use" the invention. 35 U.S.C. § 112(a). As this Court has explained, that is a standard of "reasonableness" in view of the patent's subject matter. Where a patent claim covers many different potential embodiments, the specification's instructions must be sufficiently robust to permit skilled artisans to reasonably

make and use individual embodiments *as needed*. Patent claims need not be so narrow that skilled artisans can make *all* embodiments, seriatim, with minimal time and effort.

B. The statutory "make and use" standard, and this Court's cases applying that standard, fully address the Federal Circuit's concerns about overbroad patent claims. If a claim truly exceeds what the patent enables, challengers will be able to produce evidence showing they cannot reasonably "make and use" the invention by following the patent's teachings.

III. Amgen's patents satisfy any proper formulation of § 112's enablement standard. Skilled artisans can make the 26 antibodies identified in the patents by amino-acid sequence. They can also make other antibodies within the claims by following the patents' "roadmap" and its instructions on conservative substitution, both of which employ methods routine in the antibody arts. Sanofi-Regeneron was given a retrial for the purpose of introducing evidence of specific, actual antibodies not enabled by Amgen's patents. But it failed to identify even *one* actual antibody within the claims that could *not* be made following the patents' disclosures.

## ARGUMENT

### I. THE FEDERAL CIRCUIT'S REACH-THE-FULL-SCOPE STANDARD DEFIES TEXT, PRECEDENT, HISTORY, AND POLICY

This Court has emphasized that the Patent Act is a statute and must be read as such. *Bilski* v. *Kappos*, 561 U.S. 593, 602-603 (2010). The Federal Circuit's "enablement" standard cannot be reconciled with the Patent Act's text. It defies precedent, history, and policy as well.

### A. The Federal Circuit's Reach-the-Full-Scope Standard Finds No Support in § 112

Section 112(a) states:

> The 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 * * * .

35 U.S.C. § 112(a) (emphasis added). Those requirements are straightforward. Section 112(a) mandates a disclosure: The "specification shall contain a written description." The description must be "of the invention." It must be "of the manner and process of making and using" the invention. And it must be "in such full, clear, concise, and exact terms as *to enable* any person skilled in the art * * * *to make and use* the" invention. "The object" of that enablement requirement "is to require the patentee to describe his invention so that others may construct and use it" after the patent expires. *Schriber-Schroth Co.* v. *Cleveland Tr. Co.*, 305 U.S. 47, 57 (1938).

1. That statutory standard—sufficiently "full, clear, concise, and exact * * * as to enable" skilled artisans "to make and use" the invention—is so clear that this Court applies it directly. See, *e.g.*, *Loom Co.* v. *Higgins*, 105 U.S. 580, 586 (1882) (evaluating whether patentee "describe[d] his invention in such full, clear, and exact terms as to enable persons skilled in the art to construct and use it"); *Mowry* v. *Whitney*, 81 U.S. (14 Wall.) 620, 644 (1872) (evaluating whether specification was "in such full, clear, and exact terms * * * as to enable any person skilled in the art or science to which it appertains * * * to make, construct, compound, and use the [invention]"); *Wood* v. *Underhill*, 46 U.S. (5 How.) 1, 5 (1846) ("The specification must be in

such full, clear, and exact terms as to enable any one skilled in the art to which it appertains to compound and use the invention * * * .").

This Court has described the enablement standard consistent with the statutory text. A patent's disclosure, the Court has stated, "satisfies the law" if it is "sufficiently definite to guide those skilled in the art to" the "successful application" of "the invention," *Minerals Separation, Ltd.* v. *Hyde*, 242 U.S. 261, 271 (1916); it teaches skilled artisans "to practice the invention," *Universal Oil Prods. Co.* v. *Globe Oil & Refin. Co.*, 322 U.S. 471, 484 (1944); or it "points out some practicable way of putting [the invention] into operation," *The Telephone Cases*, 126 U.S. 1, 536 (1888). If the specification teaches skilled artisans to practice the invention, that satisfies § 112's "object[ive]." *Schriber-Schroth*, 305 U.S. at 57. The patent must provide enough guidance so that skilled artisans, "following [the patent's] directions, may produce from it alone a practically operative invention." 2 W. Robinson, *The Law of Patents for Useful Inventions* § 485 (1890) ("Robinson"). It must "enable a mechanic of ordinary skill to construct it and apply it to practical use." *Aultman* v. *Holley*, 2 F. Cas. 217, 222 (C.C.S.D.N.Y. 1873).

While the specification may "leav[e] something to the skill of persons applying the invention," *Minerals Separation*, 242 U.S. at 271, it may be insufficiently "full," "clear," and "exact," 35 U.S.C. § 112(a), if skilled artisans must exercise more than ordinary skill to create an operative embodiment of the invention. The patent is "insufficient" when "independent invention would have to be exercised," *Loom Co.*, 105 U.S. at 591, because simply following the patent's directions does not produce "a practically operative invention," 2 Robinson § 485. In the now-seminal *Wands* decision, the Federal Circuit characterized that

line as one of "undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). If the required efforts exceed what "[p]ractitioners of [the] art are prepared to" undertake in the regular course, the experimentation is "undue" and the invention is not "enable[d]." *Id.* at 740.

2. The standard adopted by the Federal Circuit in this case departs from §112's text. For "genus claims" like Amgen's, the Federal Circuit imposes a "high[er] hurdle." Pet. App. 12a. Genus claims "cover[ ] a group of structurally related products that incorporate the basic advance of the patented invention," and often use "functional language" or "formulas" to encompass a class of "embodiments" that employ the inventive feature. D. Karshtedt *et al.*, *The Death of the Genus Claim*, 35 Harv. J.L. & Tech. 1, 3, 13 (2021) ("Karshtedt").

In such cases, the Federal Circuit does not merely ask whether the specification's disclosures teach skilled artisans to "make and use" the invention, 35 U.S.C. §112(a), *i.e.*, to "successful[ly] appl[y]" the invention, *Minerals Separation*, 242 U.S. at 271. Instead, it asks whether "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments." Pet. App. 14a (emphasis added); see Pet. App. 11a (effort "required to make and use, not only the limited number of embodiments the patent discloses, but also the full scope of the claim"). The court focuses on the "number of *possible candidates* within the scope of the claims"—the number of theoretical embodiments that *might* meet the claims' requirements. Pet. App. 10a (emphasis added). If the court determines that it would require "undue" effort to, one-by-one, make all or almost all the various candidates and "identify[ ]" those that "satisfy" a claim's requirements, it deems the patent invalid for lack of enablement. *McRO*

*Inc.* v. *Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 n.2 (Fed. Cir. 2020); see Pet. App. 12a.

The Patent Act contains no such how-long-to-make-them-all test. The fact that the Federal Circuit has announced a distinct test, "rais[ing] the bar" for claims it characterizes as genus claims with functional elements, Pet. App. 11a-13a—and employs other tests for other claims, see *McRO*, 959 F.3d at 1100 & n.2—makes the court's departure from the statutory text clearer still. The statute provides a single, universal enablement standard for all "invention[s]." 35 U.S.C. § 112(a). It does not provide different tests for different technologies, different claim formats, claim breadth, or the state of the art.

3. This case illustrates how far the Federal Circuit's test departs from the statutory standard. Amgen presented evidence that the patents' roadmap produces claimed antibodies *every time*, and that the roadmap will "make all the antibodies within the scope of the claims." C.A. App. 3908 (757:12-14), 3909 (762:10-20). Over 30 years ago, the Federal Circuit recognized that the techniques disclosed in Amgen's patents—immunizing mice and identifying antibodies that bind at the targeted location—are "well known" "methods for obtaining and screening monoclonal antibodies." *Wands*, 858 F.2d at 736. Because "[p]ractitioners of this art are prepared to" perform that work "in order to find * * * the desired antibody," those techniques are not "undue experimentation." *Id.* at 740.

Here, neither the Federal Circuit nor Sanofi-Regeneron identified even one actual antibody within the claims that could not be made following the patents' roadmap or that would require undue experimentation. Pet. C.A. Reply 3. Sanofi-Regeneron obtained a new trial for the purpose of presenting such evidence. But it came up empty: Testimony showed that the four antibodies Sanofi-

Regeneron proffered could be made following Amgen's roadmap. See pp. 50-51, *infra*. With respect to "conservative substitution," neither the Federal Circuit nor Sanofi-Regeneron identified a single instance in which making amino-acid substitutions specified in the patents produced a variant of a claimed PCSK9 antibody that lost its ability to bind to PCSK9's sweet spot and block PCSK9's interaction with LDL receptors. See Pet. C.A. Reply 14; see pp. 49-50, *infra*. Nor did the Federal Circuit or Sanofi-Regeneron identify information missing from Amgen's patents that left skilled artisans to conduct undue experimentation to make and use claimed antibodies.

The Federal Circuit nevertheless ruled that every reasonable juror would be compelled to find that Sanofi-Regeneron had clearly and convincingly proved the claims not enabled. Pet. App. 14a-15a. Instead of focusing on the depth of information the patents provided, and whether skilled artisans could "produce from it alone a practically operative invention," 2 Robinson §485, the court turned enablement into a numbers game. The court emphasized that Amgen's patents provided only "twenty-six examples" of antibodies described by amino-acid sequence while claiming many more. Pet. App. 8a. And it noted that the 26 example antibodies do not bind to each of the 15 amino acids in the sweet spot, and that none binds to more than nine. Pet. App. 13a & n.1. The Federal Circuit posited "millions of candidates," beyond the "disclosed examples," that *might* fall within the claims, each of which would have to be "generate[d] and then screen[ed]" to determine whether it met the claims. Pet. App. 14a-15a.

The Federal Circuit thus failed to identify any actual problem skilled artisans face in *practicing* the invention. Instead, it looked to how much "'time and effort' would be

required" for skilled artisans "*to reach the full scope* of claimed embodiments," Pet. App. 14a (emphasis added)—*i.e.*, the cumulative effort necessary to identify and make all or nearly all variations within the genus—no matter how theoretical or speculative any variation might be. While the Federal Circuit denied "hold[ing] that the effort required to *exhaust* a genus is dispositive," *ibid.* (emphasis added), it at least ruled that enablement depends on the cumulative effort required to make and use some large, but unspecified, range of embodiments. Courts, it declared, must examine the effort "required to make and use, not only the limited number of embodiments the patent discloses, but also the full scope of the claim." Pet. App. 11a.

That "dramatically" changes enablement law, "to the point where it is nearly impossible to maintain a valid genus claim." Karshtedt, at 1. The law has long been clear that, no matter the size of the claimed genus, the "applicant is not required to describe all possible forms in which [the invention] may be reduced to practice." 2 Robinson § 485. That task is "[p]lainly * * * impossible," *Mowry*, 81 U.S. at 645, for all but the narrowest inventions. Enablement asks *not* whether there is a large delta between the number of examples the patent discloses and the number of embodiments potentially covered by the claims. It asks whether the patent teaches skilled artisans to "make and use" the invention, including embodiments not specifically exemplified.

4. The Federal Circuit did not attempt to justify its reach-the-full-scope standard by reference to § 112's text. It stated that its "focus[] on the [invention's] breadth" "emerges from" the Federal Circuit's—not this Court's—"case law." Pet. App. 11a.

Without expressly endorsing the reach-the-full-scope standard, the government appears to posit a statutory basis for it. The government emphasizes that § 112 requires that the specification teach skilled artisans to make and use "'the *invention*.'" CVSG.Br. 16 (quoting 35 U.S.C. § 112(a)). It notes that, when the claim covers a genus, "the patent must enable that entire genus." *Ibid.* Sanofi-Regeneron similarly asserts that § 112(a) is not satisfied "if the patent describes how to make and use only *part* of the invention." Br. in Opp. 30. But no one denies that a patent must reasonably enable the entire scope of the claim—there cannot be large tracts of claimed subject matter that are not enabled. The problem is that the Federal Circuit requires something else entirely. It imposes a standard that looks to the number of claimed embodiments and the cumulative "time and effort" to "reach" *every* (or nearly every) embodiment within the claim—to identify and make them all—a categorically different and exponentially more demanding standard than § 112 imposes.

Any such view of § 112 rests on an extraordinary rather than ordinary understanding of what it means to "make and use the invention." In ordinary understanding, that phrase means being able to produce and employ physical versions of the invention as needed. It would not ordinarily mean that one can "make and employ every possible variation of the invention *in succession*" without expending much time or effort in the process. For example, there are nearly limitless variations of the airplane. Different materials, wing configurations, body styles, means of propulsion, etc., are possible; some of the variations might entail further inventions, *e.g.*, the jet engine. But no one would think that skilled aeronautical engineers cannot "make and use" the airplane simply because one cannot

sequentially or simultaneously build and utilize *every* conceivable variation (or improvement) without "'substantial time and effort.'"

Section 112's point is practical: to ensure that inventors, in their patents, teach the world to make and use their inventions. Section 112 thus requires a "written description" of how to make and use the invention—one that is both "clear" and "concise." 35 U.S.C. § 112(a). Examining the cumulative effort to make every or virtually every variant of the invention in succession would be a bizarre way of evaluating the sufficiency of that description. No one has identified a practical reason artisans would want or need to make all variations of the invention, collectively, without "'substantial time and effort.'" The proper test for enablement asks whether artisans can "make and use" the invention in a practical sense—whether they are able to put the claimed inventive concept into practice, as needed. If no one identifies even one, actual claimed embodiment that requires undue experimentation to "make and use" when following the patent's instructions, as here, the jury is entitled to find the claims enabled. The presumption of validity is not overcome. 35 U.S.C. § 282(a). And lack of enablement surely has not been proved by clear-and-convincing evidence. *Microsoft Corp.* v. *i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011).

### B. This Court's Precedents Refute the Federal Circuit's Test

This Court has long appreciated that, while patent claims recite "'[t]he principle of the invention,'" "'the modes of [the invention's] embodiment'" in "'concrete'" form "'may be numerous and in appearance very different from each other.'" *Cont'l Paper Bag Co.* v. *E. Paper Bag Co.*, 210 U.S. 405, 418-419 (1908) (quoting 2 Robinson § 485). Nonetheless, "it is not necessary to * * * describe

in the specification[ ] all possible forms in which the claimed principle may be reduced to practice." *Smith* v. *Snow*, 294 U.S. 1, 11 (1935). The Court has never suggested that enablement turns on the "'time and effort'" that would be required "to reach the full scope," Pet. App. 14a, identifying and making all of a claimed invention's potentially numerous embodiments.

1. This Court's decision in *Wood* v. *Underhill* forecloses any such reach-the-full-scope standard. The patent in that case was for an "improvement in the art of manufacturing bricks and tiles" that involved mixing coal dust and clay. 46 U.S. at 4. The Court acknowledged there were "variations" in types of clay. *Id.* at 5. The patent, however, did not specify the ratio of coal dust for each type. *Ibid.* It provided "a certain proportion as a general rule," but called for variation: Clay "which requires the most burning will require the greatest proportion of coal-dust," it stated; "some clay may require one eighth more than the proportions given, and some" clay a still different amount. *Ibid.*

The lower court took the case from the jury based on its determination that "the specification was too vague and uncertain to support the patent." 46 U.S. at 5-6. This Court reversed. *Id.* at 6. While the patent mentioned two departures from its general proportion of clay and coal dust, the Court regarded those as "exceptions" for clay with "some peculiarity." *Id.* at 5. The Court explained that it would be proper to take the case from the jury only if "the improvement cannot be used with advantage in *any* case, or with *any* clay, without first ascertaining by experiment the proportion to be employed." *Ibid.* (emphasis added). Because that "d[id] not appear to be the case," the Court held *the jury* must determine whether the specification's "description" of the invention was "so full, clear, and

exact as to enable any one skilled in the art to compound and use it." *Id.* at 5-6. It did not hold, as the Federal Circuit requires, that enablement turned on the "'time and effort'" necessary "to reach the full scope" by determining the proportion of coal dust required for *every* variation skilled artisans might use.

2. *Mowry* similarly defies the notion that enablement depends on the time and effort needed to "reach" the full range of embodiments. See 81 U.S. at 644-645. There, the patent's claimed process for manufacturing railway wheels avoided "strain" that results from different wheel parts cooling at different rates. *Id.* at 625-626. The patent disclosed removing the wheel from the mold before it "cooled [so much] as to produce such inherent strain on any part as to impair" the wheel; reheating the wheel so that all parts were equal temperature; and then cooling all parts "with equal slowness." *Id.* at 628-629, 641. The patent stated that the process could be applied to wheels of "any form," whether made with "spokes" or "disks connecting the rim and hub." *Id.* at 628.

The Court recognized it was "[p]lainly * * * impossible to describe" the specific temperature at which every wheel would experience strain, requiring removal from the mold and reheating. 81 U.S. at 645. Depending on structure, "thick and thin parts" will be in "different stages of cooling." *Ibid.* The timing and reheating temperature required for each wheel type were thus "left to the judgment of the operator." *Id.* at 646. Yet the Court found the patent enabled because the operator, "in following the directions of the specification, would be taught by his practical knowledge" how to successfully apply the method to a particular wheel. *Ibid.*

3. *Minerals Separation* is to the same effect. To improve the process for the "'concentration of [metallic]

ores,'" the invention involved adding oil to the ore and agitating the mixture. 242 U.S. at 263, 265. This Court explained that "each" type of ore "present[s] its [own] special problem." *Id.* at 271. The "amount of oil and the extent of agitation necessary in order to obtain the best results" would vary for each type of metal. *Id.* at 270. The patent, however, did not explain how to alter those variables for the "infinite[ ]" varieties of ore; skilled artisans would have to conduct "preliminary tests" to identify the "precise treatment" for each. *Id.* at 270-271.

The patent in *Minerals Separation* would fail the Federal Circuit's reach-the-full-scope test: The "'time and effort'" necessary for skilled artisans to identify every iteration for the "infinite" ore varieties would have been enormous. But this Court upheld the patent, explaining that "it is obviously impossible to specify in a patent the precise treatment" for each variation. 242 U.S. at 271. The statute's demands are "not greater than is reasonable, having regard to [the patent's] subject-matter." *Id.* at 270. It was enough that skilled artisans could apply the process to particular ores as needed. *Id.* at 271.

### C. Centuries of Enablement Practice Refute a Reach-the-Full-Scope Test

The Federal Circuit's reach-the-full-scope standard also departs from longstanding practice, from the decisions of Framing-era English courts to the decisions of the Federal Circuit's predecessors. That "two centuries" of courts never articulated a reach-the-full-scope test "tends to negate the existence of" any such standard. *Printz* v. *United States*, 521 U.S. 898, 918 (1997).

1. At the time the Patent Act of 1790 was enacted, English courts in "'enablement' cases" simply asked juries "to determine whether the specification described the invention well enough to allow members of the appropriate

trade to reproduce it." *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 379 (1996). In *Arkwright* v. *Nightingale*, Dav. Pat. Cas. 37 (C.P. 1785), for example, Lord Loughborough instructed the jury that a patent's "specification" must be "so intelligible, that those who are conversant in the subject are capable of * * * perpetuating the invention." *Id.* at 56; see E.W. Hulme, *On the History of Patent Law in the Seventeenth and Eighteenth Centuries*, 18 L.Q.R. 280, 284-285 (1902) (jury instructed to decide "whether the specification is such as instructs others to make it"). Juries were not asked to decide how long it would take to identify and make the invention's every embodiment.

Early English courts upheld patents that would have flunked the Federal Circuit's reach-the-full-scope test. In *Neilson* v. *Harford* (1841) 151 Eng. Rep. 1266 (Exch.), the Court of Exchequer considered Neilson's patent "for the improved application of air to produce heat in fires, forges, and furnaces, where bellows or other blowing apparatus are required." *Id.* at 1267. Neilson's patent claimed "interposing a receptacle for heated air between the blowing apparatus and the furnace." *Id.* at 1273. The patent was not limited to specific receptacles, stating that the receptacle's "size" and "shape" "may be adapted" as "necessary." *Id.* at 1273-1274. Nor was the receptacle limited to any particular material, but "'may be conveniently made of iron'" or "'other metals or convenient materials.'" *Id.* at 1267. And the patent taught that any "manner of applying the heat to the air-vessel" may be used, "if it be kept at a proper temperature." *Ibid.* The number of embodiments of the invention was limitless.

Addressing enablement, the Court of Exchequer did not calculate the time and effort required for skilled artisans to employ every distinct iteration. Instead, it stated

that, "[t]o be valid," patents need only provide a description that, "if fairly followed out by a competent workman, without invention or addition, would produce the machine for which a patent [was] taken out." 151 Eng. Rep. at 1274.

2. Early American circuit cases were similar. In *Carver* v. *Braintree Manufacturing Co.*, 5 F. Cas. 235 (C.C.D. Mass. 1843), Justice Story addressed an enablement challenge to a patent for "'a new and useful improvement in the ribs of the cotton gin'" that was designed to reduce clumping during the ginning process. *Id.* at 235-237. The patent described "the thickness of the rib" as being "so great as to be equal to the length of the fibre to be ginned." *Id.* at 236. The challenger argued the description did not "enable a mechanic to make" the invention, because "the fibres of different kinds of cotton are of different lengths." *Id.* at 237. Justice Story explained that the proper question was "[w]hether a skilful mechanic could from this description make a proper rib for *any particular kind of cotton*" as needed. *Ibid.* (emphasis added). It did not matter how long it would take a skilled artisan to make proper ribs for *every kind of cotton* that might be used.[4]

Hewing to statutory text, historic treatises confirm that the specification need only "enable an artist, skilled in the subject, to make the thing." W. Phillips, *The Law of Patents for Inventions* 237 (1837); see also G. Curtis, *A Treatise on the Law of Patents for Useful Inventions* § 124 (1849) (similar). The "modes of putting an invention to practical use," they recognize, are "often numerous and varied," even for non-genus claims. 2 Robinson § 486. But enablement merely requires the inventor to provide "di-

[4] See also *Bowker* v. *Dows*, 3 F. Cas. 1070, 1071 (C.C.D. Mass. 1878) (patent enabled where embodiments "may be varied within pretty wide limits without affecting the result," if individual variations "may be ascertained very readily" by skilled practitioners).

rections" for skilled artisans to "produce * * * a practically operative invention." *Id.* §485. That having been done, "all *other possible modes are assumed to be suggested* by it, unless they depend upon the further exercise of inventive skill, in which case they become new and separate inventions." *Id.* §486 (emphasis added). The time and effort to work out all of the various forms the invention might take is not part of the calculus.

3. Before the Federal Circuit's formation, the regional circuits shared the same view. The question, they observed, is whether "the disclosure is sufficient to enable one skilled in the art to practice the invention." *Toledo Rex Spray Co.* v. *Cal. Spray Chem. Co.*, 268 F. 201, 204 (6th Cir. 1920); see also *Donner* v. *Am. Sheet & Tin Plate Co.*, 165 F. 199, 206 (3d Cir. 1908); *Philip A. Hunt Co.* v. *Mallinckrodt Chem. Works*, 177 F.2d 583, 585 (2d Cir. 1949); *Ill. Tool Works, Inc.* v. *Foster Grant Co.*, 547 F.2d 1300, 1309 (7th Cir. 1976). Petitioners have found no case imposing a standard that examines how long it takes to make every embodiment within the claims.

To the contrary, the courts of appeals routinely upheld claims that would be invalidated under the Federal Circuit's reach-the-full-scope test. See, *e.g.*, *Franc-Strohmenger & Cowan, Inc.* v. *Arthur Siegman, Inc.*, 27 F.2d 785, 785-786 (2d Cir. 1928) (patent for class of neckties with a "resilient lining" to prevent "breaking of the stitching or distortion of the tie" enabled even though "it may require some experimentation to determine in each case what lining will do and what degree of looseness in the stitching"); *Ansul Co.* v. *Uniroyal, Inc.*, 448 F.2d 872, 877-878 (2d Cir. 1971) (claim for method of treating "growing plants" with "maleic hydrazide" to inhibit growth satisfied §112 even though "growing plants" "encompass[ed] the entire plant kingdom").

The Federal Circuit's predecessor—the Court of Customs and Patent Appeals—likewise described § 112's "essence" as the requirement "that a specification shall disclose an invention in such a manner as will enable one skilled in the art to make and utilize it." *In re Gay*, 309 F.2d 769, 772 (C.C.P.A. 1962). Thus, in *In re Angstadt*, 537 F.2d 498 (C.C.P.A. 1976), the C.C.P.A. cited *Minerals Separation* as "aptly" rejecting the notion that enablement requires more than "'guid[ing] those skilled in the art'" to the invention's "successful application." *Id.* at 503-504 (quoting *Minerals Separation*, 242 U.S. at 271). *Angstadt* concerned a method for catalytically oxidizing a genus of hydrocarbons to form hydroperoxides, using catalyst complexes. *Id.* at 499. The court found the chemical processes to be "unpredictable," and the inventor had "not disclosed" from thousands of possibilities "*every* catalyst which will work." *Id.* at 502. To identify and disclose all working catalysts would require "a prohibitive number of actual experiments." *Id.* at 502-503.

The claims were enabled nonetheless. "[P]ersons skilled in this art," the court explained, "would know how to perform processes within the scope of the claims, within the ambit of the types and amount of experimentation which the uncertainty of this art makes inevitable." 537 F.2d at 504. The court saw "no reason" why the patentees "should not be able to claim as their invention the broad range of processes" encompassed by the claims. *Ibid.*; see *In re Halleck*, 422 F.2d 911, 912, 914 (C.C.P.A. 1970) (upholding patent claiming a class of "peristalsis-regulating substances for growth stimulation" in "all types of animals and poultry").

### D. The Federal Circuit's Reach-the-Full-Scope Standard Defies Patent-Law Policy and Harms Innovation

The Federal Circuit's departure from text, precedent, and history is not only wrong. It serves no valid patent-law policy, and impedes rather than promotes innovation.

1. The "patent system represents a carefully crafted bargain that encourages both the creation and the public disclosure of new and useful advances in technology, in return for an exclusive monopoly for a limited period of time." *Pfaff* v. *Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998). Section 112 offers patent protection in exchange for "describ[ing] [the] invention so that others may construct and use it" after the patent expires. *Schriber-Schroth*, 305 U.S. at 57. The Federal Circuit's reach-the-full-scope standard reneges on that bargain. It denies an inventor a patent even if it teaches the world *exactly* how to "make and use" the invention, 35 U.S.C. § 112(a), simply because courts can speculate about "far corners" of the genus, or the time and effort that might be required to identify what the court deems "enough" variations, Pet. App. 65a. That rule refuses to reward the inventor in favor of rewarding the copyist who profits from following the patent's teachings to make yet another variation.

The Federal Circuit's rule does nothing to "promote the Progress of Science." U.S. Const. art. I, § 8, cl. 8. Once an invention has been described sufficiently for skilled artisans to make and use it, disclosing thousands more examples of variations that achieve the same result contributes little to the store of human knowledge. The act of "describ[ing] all possible forms in which" a claimed invention "may be reduced to practice * * * belong[s] to the skill of the mechanic, not the inventor." 2 Robinson § 485.

Worse still, the Federal Circuit's reach-the-full-scope test destroys incentives for breakthrough inventions. The more pioneering the innovation, the more likely it is to have a broad range of applications. Under the Federal Circuit's test, however, the more numerous and varied an invention's applications, the more likely the patent will be found invalid because "'substantial time and effort' would be required to reach the full scope of claimed embodiments." Pet. App. 14a. The test is "impossible" to satisfy whenever a claim covers a "nontrivial" number of embodiments. Karshtedt, at 4. It makes no sense to deny groundbreaking innovations patent protection because they somehow have *too many* useful implementations.

Sanofi-Regeneron insists that broad patent claims "'preempt[] the future'" by deterring innovation within the claims' scope. Resp. C.A. Br. 53. But protecting the full breadth of a breakthrough invention does not "preempt" later inventors from making improvements and securing their own patents. "[N]ew and useful improvements on" an invention are themselves "proper subjects of an application for a patent." *Seymour* v. *Osborne*, 78 U.S. (11 Wall.) 516, 548 (1871). The Federal Circuit acknowledges that "[t]here is no inconsistency in awarding a generic [claim] to one inventor, while awarding a patentably distinct species [claim] to another." *Utter* v. *Hiraga*, 845 F.2d 993, 998 (Fed. Cir. 1988). The foundational principle of the patent system, expressed in the Constitution, is to advance the progress of science by providing incentives for inventors to discover and disclose their inventions so that others can build and improve upon them. Upholding patent claims covering the invention's breadth furthers that pursuit and spurs others to pursue discoveries in the field.

2. The Federal Circuit's reach-the-full-scope test has devastating consequences. It threatens genus claims in any field whenever they cover more than disclosed examples. See, *e.g.*, *Ex Parte Beall*, No. 2020-001026, 2021 WL 1208966, at *3 (P.T.A.B. Mar. 26, 2021) (invoking decision below in invalidating genus claim in glass-making field). The impact on incentives to innovate is particularly severe in the biotech and pharmaceutical industries.

In both, breakthroughs often involve identifying the mechanism for producing a desired effect and making a working version. The inventive mechanism, however, may have the same effect when implemented in any number of structurally related compounds. Antibodies, for example, consist of chains of amino acids, many of which can be changed through routine processes without altering function—such as the process of "conservative substitution" Amgen's patents disclose. See pp. 14-15, *supra*; see also *Moba, B.V.* v. *Diamond Automation, Inc.*, 325 F.3d 1306, 1325 (Fed. Cir. 2003) (Rader, J., concurring). First-movers legitimately seek to protect their inventions through claims that use "functional language or generic formulas to cover individual embodiments of the invention, or species, that share a common attribute." Karshtedt, at 13 (footnote omitted).

Such claims are essential to offering patent protection commensurate with the invention's scope. Where the invention may take many forms, claims covering only specific versions do not provide "protection on the fruits of [the inventor's] investment." Pet. App. 65a. Copyists can "avoid infringement" simply by making a "minor change" while "still exploiting the benefits of [the] invention." *Enzo Biochem, Inc.* v. *Gen-Probe, Inc.*, 323 F.3d 956, 966 (Fed. Cir. 2002). Such follow-on products profit from the patentee's invention, which has "already * * * delivered"

the "proof of concept," without any significant scientific contribution of their own. K. Nickisch *et al.*, *How Can Pharmaceutical and Biotechnology Companies Maintain a High Profitability?*, 15 J. Com. Biotech. 309, 311 (2009).

In a field where success requires years of research and, on average, a $2.59 billion investment to bring a new product to market—Amgen here spent more than $2.7 billion—such free-rider issues undermine incentives to innovate. See J. DiMasi *et al.*, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. Health Econ. 20, 20 (2016). The Nation's leading biopharmaceutical innovators, including Bristol-Myers Squibb, Merck Sharp & Dohme, GlaxoSmithKline, and BioGen attest that the reach-the-full-scope requirement "destroy[s] value in countless" already-patented inventions, and "undermine[s]" "incentives" for companies "to invest in new discoveries." GSK. Cert. Br. 3.

3. The Federal Circuit's rule threatens to render the cost of patent protection prohibitive—and to delay disclosure of new inventions. The only way to forfend speculation about the effort to make and use all embodiments is to disclose the making and using of a large number of them. But rote identification of permutations within an invention adds nothing to the understanding in the relevant field and only results in delayed patent filings and escalating costs—costs that may squeeze out smaller innovators entirely. See *Moba*, 325 F.3d at 1325-1326 (Rader, J., concurring). Those resources would be better spent pursuing the next breakthrough than making the 1,000th example to disclose in a patent application.

Innovators who attempt to document myriad embodiments thus will face incentives to keep their inventions secret until they have completed that task. That is the op-

posite of the Patent Act's aim to spur advances in technology by encouraging inventors to timely disclose their inventions: "[F]oster[ing] concealment rather than disclosure of inventions" is contrary to "one of the primary purposes of the patent system." *Graver Tank & Mfg. Co.* v. *Linde Air Prods. Co.*, 339 U.S. 605, 607 (1950).

## II. THE STATUTORY "MAKE AND USE" STANDARD SHOULD GOVERN

Congress provided that a patent's description must be sufficient "to enable any person skilled in the art * * * to make and use" it. 35 U.S.C. § 112(a). This Court has consistently held that patent disclosures "satisf[y] the law" if they are "sufficiently definite to guide those skilled in the art to" the "successful application" of "the invention." *Minerals Separation*, 242 U.S. at 271. The "certainty which the law requires" for enabling "variations" is "not greater than is reasonable, having regard to [the patent's] subject matter." *Id.* at 270; cf. *Nautilus, Inc.* v. *Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014) (citing *Minerals Separation* in adopting "reasonable certainty" standard for indefiniteness under § 112(b)). The specification thus may "leav[e] something to the skill of persons applying the invention." *Minerals Separation*, 242 U.S. at 271.

### A. The Statute Provides a Practical Test

The enablement standard does not change when "the modes of [the invention's] embodiment'" in "'concrete'" form "'may be numerous and in appearance very different from each other.'" *Cont'l Paper Bag*, 210 U.S. at 418-419. So long as the instructions on how to make and use the invention are sufficiently robust to permit skilled artisans to practice claims as needed, without resort to undue experimentation, the claims are enabled. See pp. 29-32, *supra*. That the patent's claims can be practiced through more embodiments "than the [patent's] disclosed exam-

ples," Pet. App. 13a, is itself of no moment. "[D]escrib[ing] all possible forms in which" a claimed invention "may be reduced to practice * * * belong[s] to the skill of the mechanic, not the inventor." 2 Robinson § 485.

Application of the statutory standard reflects a *practical* inquiry into what skilled artisans *can do* using the patent's specification—not a theoretical inquiry into hypothetical applications. It enforces the requirement that the patentee disclose enough so the public can practice the invention after the patent expires. The Federal Circuit's reach-the-full-scope rule abandons that "practical focus on whether others could make use of the claimed invention" in "favor of a fruitless search for the exact boundaries of that invention." Karshtedt, at 4. It is anything but a "reasonable" standard for enablement. *Minerals Separation*, 242 U.S. at 270. The Federal Circuit's musing that there *might* be undisclosed antibodies at the "far corners of the claimed landscape that were particularly inaccessible or uncertain," Pet. App. 65a, disregards the requirement of "reasonable" enablement with due consideration for the nature of antibody science. It also disregards the clear-and-convincing burden of proof required to invalidate a patent claim. *i4i*, 564 U.S. at 95. Real evidence, not speculation, is needed to satisfy that demanding standard.

The U.S. Patent and Trademark Office ("USPTO") thus instructs its examiners that *Minerals Separation* supplies the proper "standard for determining whether the specification meets the enablement requirement." *Manual of Patent Examining Procedure* § 2164.01 (9th ed., Rev. 10, June 2020). The USPTO asks whether "the experimentation needed to practice the invention [is] undue or unreasonable." *Ibid.* "With respect to the breadth of a claim, the relevant concern is whether the scope of enablement provided to one skilled in the art by the disclo-

sure is commensurate with the scope of protection sought by the claims." *Id.* §2164.08. "[T]he scope of enablement," the USPTO explains, "must only bear a 'reasonable correlation' to the scope of the claims." *Ibid.* The USPTO has issued thousands of patents for genus claims based on this Court's guidance and that standard.

That standard has operated in U.S. courts—and in English law from which the enablement requirement derives—throughout history. When asked to adopt a reach-the-full-scope standard like the Federal Circuit's, English courts refused. In *FibroGen Inc.* v. *Akebia Therapeutics Inc.* [2021] EWCA (Civ) 1279 (Eng.), the Court of Appeal for England and Wales held that patents claiming "a class of compounds defined in structural and functional terms for use in the treatment of" anemia were enabled, even though the class was "staggeringly large." *Id.* ¶¶4, 44, 281-284, 292. The Court of Appeal rejected the lower court's theory—akin to the Federal Circuit's—that a patent is not enabled if skilled artisans cannot "identify *substantially all* compounds covered by the claim without undue burden." *Id.* ¶40 (emphasis added). Such analysis, the Court of Appeal observed, imposes "an impossible task." *Id.* ¶66. The proper standard was to ask whether a skilled person could: (1) "identify *some* compounds beyond those named in the patent" that are "within the claimed class"; and (2) undertake this process "substantially anywhere within the whole claim." *Id.* ¶97 (emphasis added). Because the process of identifying useful compounds was "routine for the medicinal chemist and iterative in nature," the claims were enabled. *Id.* ¶142; see *Dipeptidyl-Peptidase-Inhibitoren*, BGH, Sept. 11, 2013, X ZB 8/12 (Ger.) (reversing invalidation of claim encompassing class of compounds effective at reducing blood sugar levels on similar grounds).

Consistent with those standards, defendants challenging validity may prove failure to enable in several ways. They may prove that skilled artisans, using the specification, cannot construct the claimed invention at all. *Beidler* v. *United States*, 253 U.S. 447, 453 (1920) (claim not enabled where "the only form of construction of the machine and the only method of operation * * * disclosed in the patent" did not produce the claimed result). They may prove that the disclosures are insufficient in certain details to produce the invention without experimentation that exceeds what skilled artisans typically do, forcing them to invent in their own right just to create an operative embodiment. See *Consol. Elec. Light Co.* v. *McKeesport Light Co.*, 159 U.S. 465, 472-474 (1895); pp. 45-48, *infra*. The claims may also fail to enable a distinct category of embodiments that are produced or operate through a different mechanism. For example, a claim to a "side impact crash sensor" covering both mechanical and electronic sensors may not be enabled where the patent does not teach skilled artisans to make electronic sensors. *Auto. Techs. Int'l, Inc.* v. *BMW of N. Am., Inc.*, 501 F.3d 1274, 1285 (Fed. Cir. 2007). In such cases, it is the failure to describe how to make distinct types of embodiments that operate by different means (mechanical versus electronic)—not the number of potential variations one could produce following the patent's disclosures—that creates the potential for non-enablement.

A patent may also fail if it leaves skilled artisans "searching for a needle in a haystack" for the operative invention. *Idenix Pharms. LLC* v. *Gilead Scis. Inc.*, 941 F.3d 1149, 1162 (Fed. Cir. 2019), cert. denied, 141 S. Ct. 1234 (2021); *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1384-1385 (Fed. Cir. 2013); see Pet. App. 15a. When the "number of inoperative combinations" skilled

artisans must make before finding an operative one "becomes significant"—forcing skilled artisans to search among billions of permutations to identify anything that works—the claim is not enabled. *Atlas Powder Co.* v. *E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984). In that case, the effort to practice the invention crosses the line from the work of a mechanic following instructions, to an unreasonable demand that artisans engage in undue experimentation.[5]

### B. The "Make and Use" Statutory Standard Fully Addresses Concerns About Overbroad Claims

The Federal Circuit thought it necessary to improvise a new test because it feared § 112 might not otherwise prevent patentees from claiming more than they invented. See Pet. App. 13a. "Drawing a broad fence around subject matter, without filling in the holes," it declared, "is not inventing the genus." Pet. App. 64a. But the statute itself provides the solution to that concern. If the claim *truly* exceeds what the patent enables, challengers will always be able to show, through evidence, that skilled artisans cannot reasonably "make and use" large areas of the claimed invention by following the patent's teachings. 35 U.S.C. § 112(a).

This Court's decision in *Consolidated Electric* proved that point over a century ago. The patent claim there cov-

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[5] The government's invocation of the district court's statement that Amgen's specification left artisans to follow the same path as the inventor, CVSG. Br. 20, is specious. Among other things, Amgen's patents teach skilled artisans how to succeed, providing two anchor antibodies Amgen invented that can be used to identify any antibody that binds to PCSK9's sweet spot. See Pet. C.A. Br. 61-63. The district court's contrary view was so wrong Sanofi-Regeneron did not defend it on appeal, see Pet. C.A. Reply 6, and the Federal Circuit never mentioned it.

ered "all fibrous and textile materials for incandescent conductors" in electric lamps. 159 U.S. at 472. The specification, however, taught skilled artisans only how to make incandescent conductors using "carbonized paper." *Id.* at 467. Challenging the patent, Consolidated Electric proved that the patent's disclosures for carbonized paper were insufficient to enable the myriad other embodiments within the claim, because there was no "quality common to fibrous and textile substances generally as makes them suitable for an incandescent conductor." *Id.* at 474. Consolidated Electric showed that Thomas Edison had "examin[ed]" "over six thousand vegetable growths," showing "that none of them possessed the peculiar qualities that fitted them for that purpose." *Id.* at 472. It provided evidence of *actual* embodiments within the claims that required undue experimentation. The evidence showed that, only after conducting "painstaking experimentation," *id.* at 475, over "several months," and thousands of failures, did Edison independently discover "three species of bamboo" that were "suitable for" making an incandescent conductor, *id.* at 473.

No special legal test was needed to find that patent claim non-enabled. The Court found that, "[i]nstead of confining themselves to carbonized paper, as they might properly have done," the patentees had overreached by "mak[ing] a broad claim for every fibrous or textile material." 159 U.S. at 472. When it came to all other fibrous and textile materials, however, the patent's "written description" did not "'enable any person skilled in the art * * * to make * * * and use'" the invention. *Id.* at 474 (quoting Rev. Stat. § 4888). The specification is not "sufficiently definite to guide those skilled in the art to" the "successful application" of "the invention," *Minerals Separation*, 242 U.S. at 271, if it requires skilled artisans to

hunt for the needle that functions (a few species of bamboo) amidst a haystack of alternatives that do not.

This Court has repeatedly employed the statutory standard to address claims that exceed what the patent enables. *Béné* v. *Jeantet*, 129 U.S. 683 (1889), involved a challenge to a claim for a method of "refining * * * coarse hair" by "subjecting it to the action of chemicals." *Id.* at 684. The patent's only working example was a method using "a solution of a chlorine salt dissolved in an excess of muriatic acid." *Ibid.* The patent was not enabled, because the specification was "not full and clear enough to give one skilled in chemistry such an idea of the particular kinds and character of" other "chemicals * * * as would enable him to use the invention without having to resort to experiments of his own to discover those ingredients." *Id.* at 686. And in *Holland Furniture Co.* v. *Perkins Glue Co.*, 277 U.S. 245 (1928), this Court held that a claim covering any "starch glue" that has "substantially the same properties as animal glue" was not enabled, where the evidence showed that skilled artisans would have to engage in "elaborate experimentation" to discover starch glues with the properties of animal glue. *Id.* at 250-251, 257. In both cases, the Court found that the statutory standard was not met—the specification did not "'enable any person skilled in the art * * * to make * * * and use'" the invention as claimed. *Béné*, 129 U.S. at 685-686 (quoting Rev. Stat. § 4888); *Holland Furniture*, 277 U.S. at 257 (same).

The Federal Circuit's reach-the-full-scope rule is thus not only wrong, but wholly unnecessary. It allows clearly enabled claims to be invalidated based on speculation rather than proof. As explained below, neither Sanofi-Regeneron nor the courts identified any evidence that Amgen's patents left skilled artisans searching for a needle in a haystack to practice the invention. Skilled

artisans could use the patents' teachings to make embodiments beyond the disclosed example antibodies; they would succeed *every time*. See p. 49, *infra*. Sanofi-Regeneron failed to identify even *one* actual antibody that could not be made following the patent's disclosures. Sanofi-Regeneron thus failed to provide the sort of evidence of non-enablement the challengers produced in *Consolidated Electric*, *Béné*, and *Holland Furniture*. Under the Federal Circuit's reach-the-full-scope standard, mere speculation from Sanofi-Regeneron's expert that "'you *could be* immunizing mice for a hundred years,'" but "'[t]here *might be kind of* an antibody that you didn't come up with in that time period,'" Pet. App. 42a (emphasis added), was enough to invalidate Amgen's patents. That is not, and should not be, the law.

## III. AMGEN'S PATENTS ARE ENABLED

Under any reasonable formulation of the statutory standard, Amgen's claims are enabled. While the Federal Circuit deemed this "an unpredictable field of science," Pet. App. 13a, Amgen's patents gave those skilled in the antibody arts entirely predictable methods for actually producing the claimed antibodies. Mountains of evidence supported the jury's determination that skilled artisans can make individual antibodies across the claims' scope "without having to conduct undue experimentation." C.A. App. 2906-2907 (jury instructions); see C.A. App. 3630-3632 (verdict). Sanofi-Regeneron did not present any evidence of failed efforts to generate antibodies, much less evidence so overwhelming that *every* reasonable juror would be compelled to find that it had proved non-enablement by clear-and-convincing proof. 9B Wright & Miller, *Federal Practice & Procedure* § 2535 (3d ed.) (JMOL "for the party bearing the burden of proof is reserved for extreme cases").

It was undisputed that skilled artisans can readily make the 26 example antibodies Amgen's patents disclosed by amino-acid sequence. See, *e.g.*, C.A. App. 51-116 (Figs. 2A-3JJJ), 240 (85:9-43), 3903 (737:12-738:10). The district court found "there was substantial evidence * * * supporting a jury finding that [those] disclosed antibodies were representative of the structural diversity of the genus"—a finding the Federal Circuit did not disturb. Pet. App. 25a.

It was undisputed that, by following the patents' roadmap, skilled artisans can generate other claimed antibodies *every time*. C.A. App. 3896-3897 (709:2-711:11). The roadmap employed "routine and well-known" methods, Pet. App. 38a, including "'automated high-throughput techniques'" to generate additional antibodies "'quickly, efficiently, and cheaply,'" Pet. App. 42a; see pp. 13-14, *supra*. The basic "methods for obtaining and screening monoclonal antibodies" were so well known that, decades ago, the Federal Circuit identified them as routine processes "[p]ractitioners of this art are prepared to" perform in the ordinary course. *Wands*, 858 F.2d at 736, 740. And Amgen's expert testified that skilled artisans following the patents' roadmap "would be *certain* to make *all*" the antibodies across the claims. C.A. App. 3909 (762:10-20) (emphasis added), 3908 (757:12-14). Neither the Federal Circuit nor Sanofi-Regeneron identified *any* actual antibody that required undue experimentation to make under the patents' teachings.

The patents also taught skilled artisans how to make "variants" of the antibodies through "conservative amino acid substitutions." C.A. App. 221 (48:21-23, 48:29-33), 3917 (792:23-793:3); see Pet. C.A. Br. 17, 44-45; pp. 14-15, *supra*. That process *starts* with an antibody *already known* to satisfy the claims and allows skilled artisans to

make specific, minor changes "*without* destroying" the antibody's binding and blocking "activity." C.A. App. 221(48:23-33) (emphasis added). The Federal Circuit did not dispute that, in the words of Sanofi-Regeneron's expert, skilled artisans view such minor variants as "essentially copies of each other." C.A. App. 3788 (467:7-15); see Pet. C.A. Br. 17 & n.6. And conservative substitution, using the table provided by the patents, is another "well-known technique[ ]" "that all antibody scientists use." C.A. App. 221(48:21-23, 48:29-33), 3917 (792:23-793:3). Regeneron elsewhere acknowledges that, "[i]n general, a conservative amino acid substitution *will not* substantially change the functional properties of a protein." U.S. Patent No. 8,062,640, at 12:57-59 (emphasis added). Sanofi-Regeneron identified not one conservative substitution to a claimed antibody that destroyed its activity. It provided no evidence that would occur with any frequency. See Pet. C.A. Reply 10-17.

Those failures of proof speak loudly. Sanofi-Regeneron did not merely have a clear-and-convincing burden of proof. It obtained a second trial for the express purpose of introducing evidence of antibodies, developed after the patents' priority date, that the patents' roadmap supposedly fail to enable. *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1375 (Fed. Cir. 2017). On retrial, Sanofi-Regeneron urged that four antibodies—its own Praluent and antibodies from Merck and Pfizer—could not be made using the patents' disclosures. Resp. C.A. Br. 11-15. But the jury rejected that, for good reason: Amgen's expert explained in detail how the patents' roadmap produces each of those

four antibodies. Pet. C.A. Br. 37-38 (citing C.A. App. 3908-3909 (757:12-760:21), 3918-3919 (798:25-799:5)).[6]

In deciding enablement as "a question of law," "review[ed] without deference," Pet. App. 6a, the Federal Circuit repeatedly decided factual issues contrary to the jury's presumed findings (including on the nature of the art and the power of the roadmap's teachings). See Pet. 23; Pet. Reply 11-12; Pet. C.A. Br. 39-63. But the linchpin of the Federal Circuit's decision was its *legally* erroneous rule that patents are invalid if "'substantial time and effort' would be required *to reach* the full scope of claimed embodiments." Pet. App. 14a (emphasis added). That question has no place in the enablement analysis. Shorn of that legal error, this case does not require a third trip through the Federal Circuit. The jury was correctly instructed that enablement turned on whether skilled artisans could "make and use the full scope of the claimed invention * * * without having to conduct undue experimentation." C.A. App. 2906-2907. Supported by substantial evidence, the jury found that Sanofi-Regeneron failed to prove by clear-and-convincing evidence that Amgen's patents are non-enabled. C.A. App. 3630-3632 (verdict); pp. 16-17, *supra*. Reversal is warranted.

## CONCLUSION

The judgment of the court of appeals should be reversed.

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[6] Sanofi-Regeneron's suggestion that the Federal Circuit identified non-enabled embodiments, Br. in. Opp. 32 n.8, is erroneous. The panel identified theoretical antibodies that were not among the specification's "examples." Pet. App. 13a n.1. The court cited no evidence that such antibodies would not be readily generated under the patents' teachings.

Respectfully submitted.

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