No.

IN THE
Supreme Court of the United States

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AND AMGEN USA, INC.,
Petitioners,

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS, INC., AND SANOFI-AVENTIS U.S. LLC,
Respondents.

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

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS 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 questions presented are:

1. Whether enablement is "a question of fact to be determined by the jury," *Wood* v. *Underhill*, 46 U.S. (5 How.) 1, 4 (1846), as this Court has held, or "a question of law that [the court] review[s] without deference," Pet. App. 6a, as the Federal Circuit holds.

2. 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

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.

CORPORATE DISCLOSURE STATEMENT

Pursuant to this Court's Rule 29.6, petitioner Amgen Inc. states that it has no parent corporation and that no publicly held company owns 10% or more of its stock. Petitioners Amgen Manufacturing, Limited and Amgen USA, Inc. state that they are fully owned by Amgen Inc.

STATEMENT OF RELATED PROCEEDINGS

The following proceedings are directly related to this case within the meaning of Rule 14.1(b)(iii):

- *Amgen Inc., et al.* v. *Sanofi, et al.*, No. 2020-1074 (Fed. Cir.), judgment entered on February 11, 2021;
- *Amgen Inc., et al.* v. *Sanofi, et al.*, Civ. No. 14-1317-RGA (D. Del.), judgment entered on October 3, 2019;
- *Amgen Inc., et al.* v. *Sanofi, et al.*, No. 2017-1480 (Fed. Cir.), judgment entered on October 5, 2017; and
- *Amgen Inc., et al.* v. *Sanofi, et al.*, Civ. No. 14-1317-SLR (D. Del.), judgment entered on January 3, 2017.

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PETITION FOR A WRIT OF CERTIORARI

The Federal Circuit's decision in this case defies more than a century of this Court's precedents. Section 112 of the Patent Act requires patents to provide "a written description" that "enable[s]" skilled artisans "to make and use" the invention. 35 U.S.C. §112(a). To meet that requirement, the patent's disclosures must be "sufficiently definite to guide those skilled in the art to * * * successful application" of "the invention." *Minerals Separation, Ltd.* v. *Hyde*, 242 U.S. 261, 271 (1916). This Court has long held that whether a patent satisfies that "enablement" requirement is "a question *of fact* to be determined by the jury."

Wood v. *Underhill*, 46 U.S. (5 How.) 1, 4 (1846) (emphasis added). That comports with the practice of Framing-era English courts—and the Seventh Amendment's corresponding commands.

The Federal Circuit nonetheless holds that enablement is "a question of law" for it to decide "without deference." Pet. App. 6a; see *Raytheon Co.* v. *Roper Corp.*, 724 F.2d 951, 960 n.6 (Fed. Cir. 1983). The Federal Circuit has never performed the "'historical test'" this Court employs when determining whether an issue is a fact question for juries or a legal question for judges. *Markman* v. *Westview Instruments, Inc.*, 517 U.S. 370, 376 (1996). The Federal Circuit acknowledged that "[o]ne can reasonably ask, as Amgen does, why enablement is a question of law." Pet. App. 67a. It nevertheless "s[aw] no reason" to revisit the issue because, in its view, its "precedent is long in the tooth." Pet. App. 67a-68a. But this Court's contrary precedents are far longer in the tooth—by more than a century—and are binding on the Federal Circuit regardless.

By deciding enablement as a question of law, the Federal Circuit invades the jury's role. It sows uncertainty, as that court creates new and ever-mutating tests while deciding successive cases. Indeed, the Federal Circuit applied precisely such a recent court-made "hurdle[]" to enablement in this case. Pet. App. 12a. For "genus" claims like Amgen's, the Federal Circuit ruled, it is not enough that the patent meet the statutory requirement that it teach skilled artisans to "make and use" the invention. 35 U.S.C. § 112(a). Instead, the Federal Circuit requires that the specification allow skilled artisans "*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 is wrong. The Federal Circuit identified no reason why patent validity should depend on the *cumulative* effort required to ferret out *every* conceivable implementation of the invention. That test defies this Court's precedents, which recognize that "it is obviously impossible to specify in a patent the precise treatment" for each of the potentially "infinite[ ]" variations of a claimed invention. *Minerals Separation*, 242 U.S. at 271.

The impact on innovation is devastating, particularly for critical biotech and pharmaceutical innovations, as the Federal Circuit invalidates genus claims based on perceived size alone. See D. Karshtedt, M. Lemley & S. Seymore, *The Death of the Genus Claim*, 35 Harv. J.L. & Tech. (forthcoming 2021) (manuscript at 67) (rev. Apr. 19, 2021) ("*KLS*"), https://ssrn.com/abstract=3668014. The approach also contravenes sound policy and basic fairness, as this case illustrates. There was no dispute that Amgen's patented invention—monoclonal antibodies that dramatically reduce levels of "bad" cholesterol—was a breakthrough. There was no dispute the patents enabled skilled artisans to "make and use" those antibodies. 35 U.S.C. §112(a). They could make the 26 antibodies identified in the patent by amino-acid sequence and could make other antibodies within the claims by following the patents' step-by-step "roadmap," which employs methods routine in the antibody arts. No one—not respondents, not the court—identified even *one* actual embodiment that could *not* be made following the patents' disclosures. *Two different juries* upheld Amgen's patents against enablement challenges.

Reviewing enablement as a question of law, the Federal Circuit ruled that Amgen's patents were not enabled. Based on pure speculation, the Federal Circuit posited "millions of candidates" for antibodies 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' requirements. Pet. App. 15a. While no one identified actual embodiments that could not be made following the patents' teachings, the Federal Circuit speculated about "far corners of the claimed landscape that were particularly inaccessible or uncertain to make unenabled." 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). Setting aside that § 112 imposes no reach-the-full-scope requirement, the Federal Circuit never explained why skilled artisans—who could otherwise practice Amgen's invention—would need to practice every embodiment lurking in the claims' hypothetical "far corners." It invalidated Amgen's patents regardless. Review is warranted.

OPINIONS BELOW

The court of appeals' opinion (Pet. App. 1a-15a) is reported at 987 F.3d 1080. 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, the Court extended the time to file this petition to November 18, 2021. 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, is set forth in the Appendix (Pet. App. 69a).

STATEMENT

I. Statutory Framework

This Nation's patent laws reflect "a carefully crafted bargain." *Pfaff* v. *Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998). 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.* Once that time expires, the public can practice the invention "without restriction." *Bonito Boats, Inc.* v. *Thunder Craft Boats, Inc.*, 489 U.S. 141, 150-151 (1989). That is patent law's "*quid pro quo*." *Universal Oil Prods. Co.* v. *Globe Oil & Refin. Co.*, 322 U.S. 471, 484 (1944).

A. Section 112's "Enablement" Requirement

Section 112 of the Patent Act details 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). Inherited from Framing-era English law, the condition that patents "enable" skilled artisans "to make and use" the invention is known as the "'enablement'" requirement. *Markman*, 517 U.S. at 379. This Court has explained that a patent's 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, "point-[ing] out some practicable way of putting [the invention] into operation," *The Telephone Cases*, 126 U.S. 1, 536 (1888).

Assessing enablement requires "evidence" of what "persons skilled in the art" could achieve using the patent's disclosures. *Wood*, 46 U.S. at 6. Consistent with English Framing-era practice, see, *e.g.*, *Arkwright* v. *Nightingale*,

Dav. Pat. Cas. 37, 56 (C.P. 1785), this Court has held that enablement is "a question of fact to be determined by the jury," *Wood*, 46 U.S. at 4; see *Battin* v. *Taggert*, 58 U.S. (17 How.) 74, 85 (1854).

B. The Federal Circuit's Enablement Standards

While this Court has held that enablement is "a question of fact to be determined by the jury," *Wood*, 46 U.S. at 4, the Federal Circuit holds that enablement "is a question of law," *Raytheon*, 724 F.2d at 960 n.6, "review[ed] without deference," Pet. App. 6a.

In deciding that question, the Federal Circuit generally "requires that the [patent's] specification teach those in the art to make and use the invention without undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). Where a party seeks judgment as a matter of law, the Federal Circuit ordinarily requires "concrete identification of at least some embodiment" that cannot be made without undue experimentation. *McRO, Inc.* v. *Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020).

For "genus" claims like those at issue here, the Federal Circuit has created a special test. Genus claims are "patent claim[s] that cover[ ] a group of potential products that incorporate the basic advance of the patented invention." *KLS*, *supra*, at 2. Genus claims are a "central feature of patent law in the chemical, biotechnology, and pharmaceutical industries," where invention of a particular structure or mechanism that achieves a desired effect often can be implemented in a large number of similar chemical compounds or proteins. *Id.* at 1-2. Genus claims often recite structural elements or formulas in combination with functional language (reciting desired activity) to cover the "embodiments of the invention" sharing the common inventive feature. *Id.* at 16.

For such claims, 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 within the genus. If doing so would require "'substantial time and effort,'" *ibid.*, the patent is not enabled—even if individual embodiments of the invention can be made easily and every time, 35 U.S.C. § 112(a).

II. Proceedings Below

A. Amgen Invents and Patents Antibodies That Dramatically Lower Cholesterol

High LDL cholesterol causes heart disease, a leading cause of death. Pet. App. 3a; C.A. App. 3793 (487:24-488:4), 3678 (179:24-180:12). This case arises from patents for Amgen's breakthrough—*monoclonal antibodies* that dramatically lower LDL cholesterol levels. U.S. Patent No. 8,829,165, C.A. App. 37-420; and No. 8,859,741, C.A. App. 421-806.

1. The body removes LDL cholesterol from the bloodstream using LDL receptors on the liver. Pet. App. 3a. But PCSK9, a naturally occurring protein, can bind to LDL receptors and cause the receptors to be destroyed. *Ibid.* The antibodies Amgen invented prevent that. *Ibid.* The antibodies bind a specific region of PCSK9; by binding that region, they *block* PCSK9 from binding LDL receptors and prevent PCSK9 from causing them to be destroyed. C.A. App. 3796 (498:16-499:2), 3799 (509:9-13). That key region—the "sweet spot"—comprises only 15 of PCSK9's 692 amino acids. C.A. App. 3802 (524:10-11), 3875 (625:5-6), 3900 (724:15-16), 247 (100:5-10), 180 (Fig. 21D).

Amgen's invention required years of research and enormous investments. C.A. App. 3793 (488:8-12). Amgen designed protocols tailored to generate and select antibodies

that block PCSK9's interaction with LDL receptors. See Pet. C.A. Br. 5-9. Amgen created 384 antibodies that blocked PCSK9 from binding LDL receptors "well," and 85 that blocked the interaction by "greater than 90%." C.A. App. 236-237 (77:66-80:37), 3797-3798 (504:4-506:25).

2. Amgen obtained the '165 and '741 Patents covering its invention—a genus of monoclonal antibodies that bind one (or more) of the amino acids in PCSK9's sweet spot, and thereby block PCSK9 from binding LDL receptors. Pet. App. 3a; C.A. App. 411-412, 796-797.

Amgen's patents are a "rich handbook," providing a "wealth of information" about the claimed antibodies. C.A. App. 3910 (763:1-12). They disclose the amino-acid sequences of 26 antibodies that bind PCSK9's sweet spot and thereby block PCSK9 from binding to LDL receptors. Two juries have found that those antibodies represent the full diversity of the claimed genus. See Pet. App. 5a-6a, 25a. One of those antibodies—"21B12"—is the basis for Amgen's Repatha®, the first PCSK9 inhibitor ever approved to treat high LDL cholesterol. C.A. App. 3793 (488:18-24), 3800 (513:23-514:2).

The patents teach skilled artisans how to make claimed antibodies quickly and easily. Artisans can make the 26 example antibodies using their amino-acid sequences. See C.A. App. 51-116 (Figs. 2A-3JJJ), 240 (85:9-43). They can also follow the patents' step-by-step "roadmap," which teaches artisans to generate antibodies across the scope of the claims using "routine and well-known" techniques, including "immunizing mice," specifically tailored to produce the claimed antibodies. Pet. App. 38a-39a; see Pet. C.A. Br. 13-16. Skilled artisans can use "'automated high-throughput techniques'" to select antibodies within the claims "'quickly, efficiently, and cheaply.'" Pet. App. 42a. The patents also explain how to make "variants" of those

antibodies using "conservative amino acid substitutions," another "well-known technique[]." C.A. App. 221(48:21-23, 48:29-33); see Pet. C.A. Br. 17 & n.5.

B. Two Juries Find Amgen's Patents Valid

Amgen sued respondents Sanofi and Regeneron ("Sanofi-Regeneron") for patent infringement. Pet. App. 5a. Sanofi-Regeneron stipulated to infringement but asserted invalidity defenses under § 112, including lack of "written description" and "enablement." *Ibid.* 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 Sanofi-Regeneron's motion for JMOL. C.A. App. 2061-2065, 2885. The Federal Circuit vacated and remanded for a new trial, citing an erroneous jury instruction and evidentiary ruling. See *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1375-1382 (Fed. Cir. 2017).

After a second trial, another jury found that Sanofi-Regeneron failed to prove Amgen's patents invalid for lack of written description or enablement. Pet. App. 6a. On JMOL, the district court upheld the jury's verdict on written description, Pet. App. 23a-27a, but overturned its enablement verdict, Pet. App. 31a-44a.

C. Proceedings Before the Federal Circuit

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

1. The Federal Circuit explained that, under its precedent, "[w]hether a claim satisfies the enablement requirement of 35 U.S.C. § 112 is a question of law." Pet. App. 6a. "[A]lthough the [enablement] determination may be based on underlying factual findings" reviewed for "clear error," the Federal Circuit decides enablement itself "without deference." *Ibid.* To satisfy the enablement requirement, the court stated, the patent's disclosures

must enable skilled artisans "to make and use the full scope of the claimed" invention without "undue experimentation." Pet. App. 10a.

Despite arguing the claims were not enabled, Sanofi-Regeneron failed to identify a *single actual embodiment* within the claims that could not be made quickly and easily by following the patents' teachings. Pet. C.A. Br. 37-38. The jury heard testimony that Amgen's roadmap, using immunized mice, will "generate" antibodies within the claims every time. C.A. App. 3908 (756:8-20, 757:12-14), 3909 (762:14-20). There was *no* evidence of *any* variant made through conservative substitution that failed to work, much less evidence that failures might occur with any frequency. Pet. C.A. Br. 59; Pet. C.A. Reply 14-15.

The Federal Circuit nonetheless held Amgen's claims not enabled. Pet. App. 7a, 15a. Genus claims like Amgen's, it declared, confront uniquely "high hurdles in fulfilling the enablement requirement." Pet. App. 12a. For such claims, "'undue experimentation can include'" the effort to "'*identify*[ ]'" the various embodiments that meet the requirements of the claimed genus. *Ibid.* (emphasis added).

The court concluded that "practic[ing] the full scope of [Amgen's] claims" would require "undue experimentation." Pet. App. 15a. The court acknowledged that "[t]he parties dispute[d]" myriad factual issues at trial. Pet. App. 12a. Contrary to Amgen's evidence and the jury's verdict, however, the Federal Circuit posited that "millions of candidate[ ]" antibodies might be "encompass[ed]" by the claims; 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), 3908-3909 (757:12-762:20), 3918-3919 (798:25-799:5). The court stated that, "*to reach the full scope* of

claimed embodiments," Pet. App. 14a (emphasis added), skilled artisans would have "to first generate and then screen" every theoretical "candidate[ ]" "to determine whether it" falls within the claims, Pet. App. 15a. It ruled that "no reasonable jury could conclude * * * that anything but 'substantial time and effort' would be required" to perform that work. Pet. App. 14a. The court thus found Amgen's claims "invalid for lack of enablement." Pet. App. 15a.

2. The Federal Circuit denied rehearing and rehearing en banc. Pet. App. 60a-61a. In an opinion respecting denial joined by all panel members, Pet. App. 60a-68a, the court admitted that "[o]ne can reasonably ask, as Amgen does, why enablement is a question of law" rather than a fact question for juries. Pet. App. 67a. "But our precedent is long in the tooth," the opinion stated, "and we see no reason" for imposing "a seismic shift" in how enablement is decided. Pet. App. 67a-68a.

The opinion defended evaluating enablement based on the " 'time and effort' * * * required to reach the full scope of claimed embodiments." Pet. App. 14a; see Pet. App. 62a. Confronting the outpouring of "[a]mici and others bemoaning" that test, the concurrence denied that the court asks "how long it would take to make and screen every" embodiment within the claims. Pet. App. 63a-64a. The opinion did not reconcile that denial with the panel's holding that Amgen's patents were not enabled because "'*substantial time and effort*' would be required *to reach the full scope of claimed embodiments*." Pet. App. 14a (emphasis added). The "limited guidance in the specification," the opinion insisted, "made *far corners of the claimed landscape* that were particularly inaccessible or uncertain to make unenabled." Pet. App. 65a (emphasis added). The opinion again identified no embodiment (or even an iden-

tifiable "far corner") skilled artisans would consider "inaccessible or uncertain."

REASONS FOR GRANTING THE PETITION

Section 112's enablement requirement carried over from Framing-era English law. Consistent with English practice, this Court has long held that enablement is "a question of fact to be determined by the jury." *Wood* v. *Underhill*, 46 U.S. (5 How.) 1, 4 (1846). That holding is unambiguous. Yet the Federal Circuit holds the opposite: Enablement, it holds, is "a question of law that [judges] review without deference." Pet. App. 6a. Confronted with that conflict, the Federal Circuit admitted that "[o]ne can reasonably ask * * * why enablement is a question of law." Pet. App. 67a. It nonetheless declined to reconsider because, in its view, Federal Circuit "precedent is long in the tooth." Pet. App. 68a. But this Court's precedents go back longer, to more than a century before the Federal Circuit's creation, and are binding regardless. Those precedents and Framing-era practice make clear that juries decide, as a factual matter, whether an invention is enabled. The Federal Circuit's contrary rule invades the jury's role—with grave consequences for parties and the judicial system alike. The Federal Circuit has now made clear it will not correct course. Review is warranted.

The Federal Circuit has also rewritten the substantive enablement standard. Section 112's text is straightforward: The specification must "enable any person skilled in the art * * * to make and use" the invention. 35 U.S.C. § 112(a). This Court's articulation of the standard is equally clear: The specification must "guide those skilled in the art to" the "successful application" of "the invention." *Minerals Separation, Ltd.* v. *Hyde*, 242 U.S. 261, 271 (1916). For genus claims like Amgen's, however, the Federal Circuit has substituted a standard of its own devising.

It holds that a patent is not enabled if "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments" —*i.e.*, to cumulatively identify and make all or almost all possible antibodies that might satisfy the claims. Pet. App. 14a (emphasis added).

That standard is "impossible" to satisfy for any invention of sufficiently broad application that it encompasses a "nontrivial" number of embodiments. D. Karshtedt, M. Lemley & S. Seymore, *The Death of the Genus Claim*, 35 Harv. J.L. & Tech. (forthcoming 2021) (manuscript at 4) (rev. Apr. 19, 2021) ("*KLS*"), https://ssrn.com/abstract=3668014. The Federal Circuit thus routinely invalidates patent claims based on their perceived breadth. In this case, there was no dispute that skilled artisans could easily "make and use" antibodies within Amgen's claims. But the Federal Circuit held Amgen's patents invalid on the theory that "'substantial time and effort' would be required *to reach* the full scope of claimed embodiments." Pet. App. 14a (emphasis added). That rewrite of statutory text threatens innovation. It warrants review.

I. The Federal Circuit's Treatment Of Enablement As A Question Of Law Defies History And Precedent

The Federal Circuit holds that § 112's "enablement requirement" is "a question of law" courts "review without deference." Pet. App. 6a. But this Court—consistent with historical practice—has held the opposite, declaring enablement "a question of fact to be determined by the jury." *Wood*, 46 U.S. at 4. That conflict warrants review.

A. This Court and Others Have Long Held That Enablement Is a Question of Fact

From the Patent Act of 1790 to today, this Nation's law has required that patent disclosures "enable" skilled artisans "to make and use" the invention. Act of Apr. 10, 1790,

ch. 7, §2, 1 Stat. 109, 110-111. For more than 150 years, the law was clear: Enablement is a factual determination for a jury. In *Battin* v. *Taggert*, 58 U.S. (17 How.) 74 (1854), the Court reversed a directed verdict because "[i]t was the right of the jury to determine, from the facts in the case, whether the specifications * * * were so precise as to enable any person skilled in the [art] to make the [invention] described." *Id.* at 85. "This the statute requires," the Court concluded, "and of this the jury are to judge." *Ibid.*

Wood was clearer still. After explaining that the patent "specification" must "enable any one skilled in the art" to "use the invention," the Court ruled that "the sufficiency of the description must, in general, be *a question of fact* to be determined by the jury." 46 U.S. at 4 (emphasis added). The trial court "erred in instructing the jury that the specification was too vague and uncertain to support the patent." *Id.* at 6. "[W]hether *the fact* is so or not," the Court explained, "is a question to be decided by a jury, upon the evidence of persons skilled in the art to which the patent appertains." *Id.* at 5-6 (emphasis added).

This Court has repeatedly confirmed that whether the specification contains a "sufficient description of [the invention], and of the manner of constructing it," is a "*matter of fact for the jury* and *not of law* for the decision of the Court." *Evans* v. *Eaton*, 20 U.S. (7 Wheat.) 356, 428 (1822) (emphasis added); see *Hogg* v. *Emerson*, 52 U.S. (11 How.) 587, 606 (1850). Early circuit court decisions agreed: Enablement is a "question of fact," *Lowell* v. *Lewis*, 15 F. Cas. 1018, 1021 (C.C.D. Mass. 1817) (Story, J.), that depends "upon the judgment of the jury," *Gray* v. *James*, 10 F. Cas. 1015, 1018 (C.C.D. Pa. 1817).

Early treatises reflect the same rule. Whether the "specification [is] so clear and full, as to enable a person of

ordinary skill" to "make, compound and use" an invention, they observe, "is a question of fact." Phillips, *The Law of Patents for Inventions* 430 (1837); accord G. Curtis, *A Treatise on the Law of Patents for Useful Inventions* § 395 (1849) (enablement a "question of fact for the jury").

Before the Federal Circuit's creation, the courts of appeals overwhelmingly shared the same view: Whether a patent satisfies § 112 "is a question of fact" that, once decided, can be "disturbed only if unsupported by substantial evidence, or if otherwise clearly wrong." *Bank* v. *Rauland Corp.*, 146 F.2d 19, 22 (7th Cir. 1944); see *Tights, Inc.* v. *Stanley*, 441 F.2d 336, 342-343 (4th Cir. 1971) (citing *Battin*, 58 U.S. 74); *Gasifier Mfg. Co.* v. *Gen. Motors Corp.*, 138 F.2d 197, 198-199 (8th Cir. 1943); *Anraku* v. *Gen. Elec. Co.*, 80 F.2d 958, 963 (9th Cir. 1935). Enablement "cannot be advanced as [an issue] of law," as "[t]he jury is at liberty to apply its own view and use its own common sense about the matter." *A.B. Dick Co.* v. *Barnett*, 288 F. 799, 800 (2d Cir. 1923) (citing *Hogg*, 52 U.S. 587).

B. Framing-Era Practice Treated Enablement as a Question of Fact

Framing-era English practice reflects the same rule. Patent litigation of that era was "typified by * * * 'enablement' cases, 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* v. *Westview Instruments, Inc.*, 517 U.S. 370, 379 (1996).

Those juries decided enablement as a question of fact. In *Arkwright* v. *Nightingale*, Dav. Pat. Cas. 37 (C.P. 1785), 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. That turned on the jury's assess-

ment of *credibility*—in that case, "whether [they] believe[d] five witnesses who have sworn" that "the specification was sufficient" to "direct the making of the [patented] machine." *Id.* at 57, 60. Likewise, in *Liardet* v. *Johnson* (KB 1778), Lord Mansfield instructed the jury to decide the factual question of "whether the specification is such as instructs others to make it." E.W. Hulme, *On the History of Patent Law in the Seventeenth and Eighteenth Centuries*, 18 L.Q.R. 280, 284-285 (1902).

Such jury determinations were virtually conclusive. In *Hornblower* v. *Boulton*, Dav. Pat. Cas. 221, 224-225 (KB 1799), the jury found the "specification['s]" directions "sufficient to enable a mechanic to make the thing described" as the invention. On appeal, Justice Laurence explained that "whether those directions were or were not sufficient" was "not * * * a question for [the court's] decision; it was a question for the determination of the jury, and they have decided it." *Id.* at 239-240; see *Boulton* v. *Bull*, 2 H. Bl. 463, 479 (C.P. 1795). That history is clear.

As *Markman* explains, moreover, this Court applies a "'historical test'" to determine whether an issue is a fact question for juries or question of law for courts. 517 U.S. at 376. The Court assesses "whether the particular trial decision" was one that "f[e]ll to the jury" "'under the English common law when" the Seventh Amendment "was adopted.'" *Ibid.* (quoting *Balt. & Carolina Line, Inc.* v. *Redman*, 295 U.S. 654, 657 (1935)). The "clear historical evidence" shows that enablement was "regarded" as a factual "issue for a jury" under "English practice" at the Framing. *Id.* at 377. Courts thus may not re-examine any such "fact tried by a jury" except "according to the rules of the common law." U.S. Const. amend. VII.

C. The Federal Circuit Holds That Enablement Is a Question of Law

Notwithstanding those longstanding precedents, the Federal Circuit holds that compliance with "the enablement requirement of 35 U.S.C. § 112 is a question of law" it "review[s] without deference." Pet. App. 6a. The Federal Circuit adopted that rule in 1983, in a footnote. *Raytheon Co.* v. *Roper Corp.*, 724 F.2d 951, 960 n.6 (Fed. Cir. 1983). It provided no analysis. It did not mention this Court's decisions in *Battin*, *Wood*, or *Evans*. It did not perform the "'historical test'" *Markman* describes. 517 U.S. at 376. Nor did it address decisions of the regional courts of appeals.[1] The court cited decisions from its predecessor, the U.S. Court of Customs and Patent Appeals (C.C.P.A.), which assumed enablement is a "legal question." *In re Hogan*, 559 F.2d 595, 604 (C.C.P.A. 1977). But the C.C.P.A.—which reviewed appeals from the Patent Office, but not jury verdicts, see 28 U.S.C. § 1542 (1952)—offered no analysis, either.

Confronted with this Court's precedent, Pet. C.A. Br. 30; Reh'g Pet. 15-18, the Federal Circuit "s[aw] no reason" to reconsider, Pet. App. 68a. Conceding that "[o]ne can reasonably ask, as Amgen does, why enablement is a question of law," it deemed its own precedent too "long in the tooth" to disturb. Pet. App. 67a. But *this Court's* prece-

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[1] Five circuits held that enablement is a question of fact. P. 15, *supra*. While the D.C. Circuit deemed it a question of law, *Watson* v. *Bersworth*, 251 F.2d 898, 901 (D.C. Cir. 1958), it cited only *Minnesota Mining & Manufacturing Co.* v. *Carborundum Co.*, 155 F.2d 746, 749 (3d Cir. 1946). But *Carborundum* did not consider *Battin*, *Wood*, or *Evans*. Regardless, that circuit conflict further supports review. See S. Shapiro *et al.*, *Supreme Court Practice* § 4.7, at 256-257 (10th ed. 2013).

dents are *longer* in the tooth—by more than a century—and are binding on all inferior courts regardless.[2]

On rehearing, Sanofi-Regeneron argued that, under *Seymour* v. *Osborne*, 78 U.S. 516 (1870), enablement "is 'open to legal construction as to [its] sufficiency.'" Resp. Reh'g Pet. 13 (quoting 78 U.S. at 540). That quote, however, appears in a general discussion of what inventors must do "to obtain" patents from the patent office, *e.g.*, "make application in writing," provide the inventor's "oath," and include a disclosure that enables skilled artisans to practice the invention. 78 U.S. at 540. *Seymour* stated that "these several requirements may be regarded as conditions precedent" to patent issuance, adding that they "are always open to legal construction as to their sufficiency." *Ibid.* That passing comment says nothing about whether enablement of an issued patent—when raised as a defense in litigation—is a question of fact for the jury. *Seymour* did not involve enablement at all, much less purport to overrule *Battin*, *Wood*, and *Evans*.[3]

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[2] On rehearing, the panel attempted to liken enablement to obviousness. Because enablement also "involves interpreting the specification and the scope of the claims," the panel stated, it too could be deemed a "question of law"—"if one that accommodates underlying factual inquiries." Pet. App. 68a. But this Court has *held* that enablement is "a question *of fact*," *Wood*, 46 U.S. at 4 (emphasis added), and that "obviousness" is a question of law, *Graham* v. *John Deere Co. of Kansas City*, 383 U.S. 1, 17 (1966). Attempting to analogize them can no more convert enablement into a question of law than it can transform obviousness into a fact question in contravention of binding precedent. And treating enablement as a fact question makes sense: It is an inherently evidence- and credibility-based factual inquiry into what skilled artisans actually can do employing the patent's disclosures. *Wood*, 46 U.S. at 5-6; pp. 14-16, *supra*.

[3] Sanofi-Regeneron also invoked this Court's statement that "the ultimate question of patent validity is one of law," with "underlying" "fac-

Federal Circuit law is also internally incoherent. That court has construed §112(a) as imposing *two* separate requirements—(1) "'a written description of the invention'" and (2) a description that "'enable[s] any person skilled in the art * * * to make and use the'" invention. *Ariad Pharms., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (en banc) (quoting 35 U.S.C. §112). According to the Federal Circuit, the sufficiency of a patent's "written description" is "a question of fact," *id.* at 1351, but whether it "enables" skilled practitioners to "'make and use'" the invention is a question of law, Pet. App. 6a. The panel thus found it "reasonabl[e]" to ask "why enablement is a question of law when written description * * * is not," as both are derived from the *same sentence* in §112. Pet. App. 67a. The panel, however, did not answer that question. The Federal Circuit has *never* explained why written description, which involves an "objective inquiry into the four corners of the specification," *Ariad*, 598 F.3d at 1351, is a question of fact, while enablement, which turns "upon the evidence of persons skilled in the art," *Wood*, 46 U.S. at 6, is a question of law. The Federal Circuit's determinations regarding which issues are factual and which are legal are simply "inexplicable." *Anascape, Ltd.* v. *Nintendo of Am. Inc.*, 601 F.3d 1333, 1342 (Fed. Cir. 2010) (Gajarsa, J., concurring).

D. The Issue Is Exceptionally Important

Recognizing the issue's importance, the Federal Circuit characterized any course correction as "a seismic shift." Pet. App. 68a. But the "seismic shift" occurred when the

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tual questions." Resp. Reh'g Pet. 13 (citing *Microsoft Corp.* v. *i4i Ltd. P'ship*, 564 U.S. 91, 96-97 (2011)). But the "inference of law" whether a patent is *valid* follows directly "from the facts previously" decided by the jury, including whether the specification is enabling. *Grant* v. *Raymond*, 31 U.S. 218, 245 (1832).

Federal Circuit departed from this Court's precedents and historical practice. A corrective shift is required to restore juries and judges to their proper roles.

1. Critical to the fairness and integrity of our judicial system, the "sacred" right "of jury trial in civil cases" is "jealously guarded." *Jacob* v. *City of New York*, 315 U.S. 752, 752-753 (1942). The Framers protected that right in constitutional text. "[N]o fact tried by a jury," the Seventh Amendment declares, "shall be otherwise re-examined in any Court of the United States, than according to the rules of the common law." U.S. Const. amend. VII.

Enablement turns on a fundamentally factual question: Are the specification's disclosures "sufficiently definite to guide those skilled in the art to" the invention's "successful application"? *Minerals Separation*, 242 U.S. at 271. Juries are well-suited to decide that question based "upon the evidence of persons skilled in the art," *Wood*, 46 U.S. at 6, weighing conflicting expert testimony and making credibility determinations, pp. 14-16, *supra*.

By deeming enablement a question of law, the Federal Circuit licenses courts to substitute their judgments, *sub silentio*, on disputed issues that "[i]t was the right of the jury to determine." *Battin*, 58 U.S. at 85. Time and again, the Federal Circuit and district courts now reverse jury verdicts—or invalidate patents without trial—exercising their *own* judgment to hold patents not enabled "as a matter of law." *Idenix Pharms. LLC* v. *Gilead Scis. Inc.*, 941 F.3d 1149, 1162 (Fed. Cir. 2019), cert. denied, 141 S. Ct. 1234 (2021); see, *e.g.*, *Trs. of Bos. Univ.* v. *Everlight Elecs. Co.*, 896 F.3d 1357, 1364 (Fed. Cir. 2018); *Martek Biosciences Corp.* v. *Nutrinova Inc.*, 520 F. Supp. 2d 537, 558 (D. Del. 2007); see also *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1382 (Fed. Cir. 2013); *Enzo Life Scis., Inc.* v. *Roche Molecular Sys., Inc.*, 928 F.3d 1340,

1349 (Fed. Cir. 2019), cert. denied, 140 S. Ct. 2634 (2020); *KLS*, *supra*, at 67 (citing Federal Circuit cases "overturning" "jury verdict[s]" on "enablement").

The resulting harm to the judicial system is profound. It is widely perceived that, "by redefining many issues as issues of law rather than fact," the Federal Circuit has "bec[o]me a second jury by substituting its opinion for the jury verdict." T. Lee & M. Evans, *The Charade: Trying a Patent Case to All "Three" Juries*, 8 Tex. Intell. Prop. L.J. 1, 4 (1999); see L. Pedraza-Fariña, *Understanding the Federal Circuit: An Expert Community Approach*, 30 Berkeley Tech. L.J. 89, 93, 101 (2015) (noting court's "aggressive de novo review" and tendency to "act[ ] as a fact-finder"). The Federal Circuit's decisions likewise prompt concerns about "panel dependency"—the "prominent" perception that outcomes depend not on the law or the record, but on whether one draws pro-patent or anti-patent judges. C. Nard & J. Duffy, *Rethinking Patent Law's Uniformity Principle*, 101 Nw. U. L. Rev. 1619, 1627 (2007); see T. Field, *Hyperactive Judges: An Empirical Study of Judge-Dependent 'Judicial Hyperactivity' in the Federal Circuit*, 38 Vt. L. Rev. 625, 627 (2014).

2. Treating enablement as a legal question invites doctrinal uncertainty, as the Federal Circuit creates new tests when deciding enablement as a "legal" question in successive cases. Inventors cannot rely on patent protection where the Federal Circuit, under the guise of deciding legal questions, creates a mutating body of law and applies it to patents filed years earlier, when inventors had no opportunity to address that court's extra-statutory requirements.

Congress created one statutory standard: The patent's disclosures must enable skilled artisans to "make and use" the invention. 35 U.S.C. § 112(a). But the Federal Circuit

has created divergent standards depending on the patent claim. For some, it demands the party challenging enablement provide "concrete identification of at least some embodiment" that cannot be made without undue experimentation. *McRO, Inc.* v. *Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020). As explained below (at 24-32), for genus claims like Amgen's, it has created a different, heightened standard, asking whether "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments." Pet. App. 14a (emphasis added). Examining the cumulative effort to make the full scope of embodiments diverges dramatically from inquiring whether skilled artisans can make and use individual embodiments. The Federal Circuit's standard for genus claims imposes a "high hurdle[ ]" found nowhere in § 112. Pet. App. 12a

3. This case illustrates the dangers. To prevail before the jury, Sanofi-Regeneron was required "to prove" "lack of enablement * * * by clear and convincing evidence." *Alcon Rsch. Ltd.* v. *Barr Labs., Inc.,* 745 F.3d 1180, 1188 (Fed. Cir. 2014). *Two separate juries* found Amgen's claims enabled after *two trials*. Pet. App. 5a-6a. To overturn the jury verdict on appeal, Sanofi-Regeneron was required to demonstrate its case was so overwhelming that *no reasonable juror* could reject its evidence as falling short of *its clear-and-convincing burden*.

Sanofi-Regeneron urged the jury below that Amgen's claims "require undue experimentation" based on its "conten[tions] that there are millions of antibody candidates within the scope of the claims, the disclosures do not provide sufficient guidance, antibody generation is unpredictable, and practicing the full scope of the claims requires substantial trial and error." Pet. App. 9a. The jury is presumed to have sided with Amgen on each of those hotly

contested fact issues. Pet. App. 5a-6a. Deciding enablement as "a question of law," reviewed "without deference," Pet. App. 6a, the Federal Circuit exacerbated its invasion of the jury's role by reaching the opposite result on each of those disputes. For example:

- The Federal Circuit acknowledged that "[t]he parties dispute[d]" the size of the claimed genus, Pet. App. 12a, with Amgen's witnesses testifying that the claims "are very narrow," C.A. App. 3883 (658:1-5); see Pet. C.A. Br. 20-21. Yet the court of appeals declared Amgen's "claims were indisputably broad," "encompass[ing] millions of candidates." Pet. App. 12a, 15a.
- Amgen's expert testified that the patents' "road map [was] not a trial and error process," because following it "generate[s] the antibodies" within the claims with "certainty" every time. C.A. App. 3908 (756:15-20). The Federal Circuit dismissed the roadmap as an "unpredictable," "trial and error" process. Pet. App. 9a.
- Amgen presented expert testimony 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). But the Federal Circuit declared that the patents do not provide "adequate guidance" beyond "the working examples" in the specification. Pet. App. 14a.

Two juries found the claims enabled. The Federal Circuit parted company with both.

In deciding enablement as a legal question, the Federal Circuit has created novel legal rules for genus claims. Applying one here, it invalidated Amgen's claims "for lack of enablement," Pet. App. 15a, because "'substantial time and effort' would be required *to reach the full scope* of

claimed embodiments," Pet. App. 14a (emphasis added). Amgen thus lost protection for its invention under an extra-textual standard—even though skilled artisans undeniably could "make and use" the invention as the statute requires. 35 U.S.C. § 112(a).

4. Review is warranted now. The Federal Circuit routinely lays waste to innovative patents that juries upheld at trial. See pp. 20-21, *supra*. It has now confirmed that it will not reconsider and align its decisions with this Court's holding that enablement is a fact question, deeming its contrary rule "indelibly embodied" in circuit law. Pet. App. 68a. It "see[s] no reason" to reconsider because, in its view, this Court has "not seen fit to take up this question" despite "repeated[ ]" requests. *Ibid.* Prior petitions, however, were plagued by vehicle issues, see, *e.g.*, Br. in Opp. 36, *Idenix Pharms. LLC* v. *Gilead Scis., Inc.*, No. 20-380 (noting "independent holdings invalidating Idenix's patents"), wholly absent here. Confronted by a case that properly presents this "seismic" question, this Court should "see[ ] fit to take up" the issue now. Pet. App. 68a.

II. THE FEDERAL CIRCUIT'S "REACH THE FULL SCOPE" STANDARD WARRANTS REVIEW

This Court has admonished the Federal Circuit not to "impose limitations on the Patent Act that are inconsistent with the Act's text." *Bilski* v. *Kappos*, 561 U.S. 593, 612 (2010). But the Federal Circuit has done it again, creating an atextual enablement standard that "raises the bar" for certain claims. Pet. App. 13a. For genus claims like Amgen's, the Federal Circuit does not ask whether skilled artisans can "make and use" the invention, as § 112 and this Court's precedents require. Instead, it invalidates genus claims if it believes "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments"—*i.e.*, to identify and make all or nearly all pos-

sible embodiments of the invention. Pet. App. 14a (emphasis added). That standard frustrates the purposes of patent law. It invalidates patents for breakthrough inventions, demanding disclosure about theoretical "far corners," Pet. App. 65a, a standard that contributes nothing to progress of the useful arts. And it has devastating consequences for innovation, particularly in the critical biotech and pharmaceutical sectors.

A. The Federal Circuit's "Reach the Full Scope" Requirement Defies Text, Precedent, and Policy

1. Section 112 requires inventors to provide "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). In the 200 years since the first Patent Act, this Court has described the enablement standard consistent with that text: The patent's 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; teach skilled artisans "to practice the invention," *Universal Oil Prods. Co.* v. *Globe Oil & Refin. Co.*, 322 U.S. 471, 484 (1944); or "point[ ] out some practicable way of putting [the invention] into operation," *The Telephone Cases*, 126 U.S. 1, 536 (1888). By doing so, patents meet §112's "object[ive]," which "is to require the patentee to describe his invention so that others may construct and use it after the [patent's] expiration." *Schriber-Schroth Co.* v. *Cleveland Tr. Co.*, 305 U.S. 47, 57 (1938).

The Federal Circuit has adopted a different enablement test for genus claims like those here. Such claims often use "functional language" or "formulas" to encompass a class of "embodiments" that employ the inventive feature. *KLS*, *supra*, at 16. In such cases, the Federal

Circuit does not ask whether there are actual embodiments skilled artisans cannot "make and use" per § 112's requirements, but whether "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments." Pet. App. 14a (emphasis added). In other words, the court considers whether "*identifying*" all various embodiments that "satisfy" the requirements of the claimed genus would require "undue" effort. *McRO*, 959 F.3d at 1100 n.2 (emphasis added).

2. The Federal Circuit's novel reach-the-full-scope test is not merely atextual. It is wrong. This Court's *Minerals Separation* decision forecloses it.

In *Minerals Separation*, the patent involved "'improvements in the process for the concentration'" of metallic ores. 242 U.S. at 263. The invention involved adding oil to the ore and agitating the mixture. *Id.* at 265. This Court recognized that 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. But the patent did not explain how to alter those variables for the "infinite[]" varieties of ore, and 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 have failed the Federal Circuit's reach-the-full-scope test: The "'time and effort'" necessary for skilled artisans "to reach the full scope" of claimed embodiments—the iterations 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. It was enough that skilled artisans could apply the process to particular ores as needed. *Ibid.* This Court regularly reached similar conclusions when addressing patent claims covering a

large number of potential embodiments. See, *e.g.*, *Wood*, 46 U.S. at 5-6 (rejecting enablement challenge to patent for "manufacturing bricks" through mix of coal dust and clay even though proportions would vary for each type of clay); *Mowry* v. *Whitney*, 81 U.S. 620, 644-645 (1871) (rejecting enablement challenge to method of cooling metal wheels even though temperature required for each embodiment was "left to the judgment of the operator").

3. The Federal Circuit's reach-the-full-scope standard serves no valid patent-law policy. The patent bargain requires "the patentee to describe his invention so that others may construct and use it after the expiration of the patent." *Schriber-Schroth*, 305 U.S. at 57. The Federal Circuit's reach-the-full-scope requirement, by contrast, "abandon[s] a 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." *KLS*, *supra*, at 4. There is no reason to demand that skilled artisans be able to identify and make all potential embodiments within the claims with minimal "'time and effort.'" Pet. App. 14a. Respected commentators thus urge that "[t]he validity of a claim should not depend on whether others can identify and test *all*" embodiments of a genus claim. *KLS*, *supra*, at 4.

The Federal Circuit's disclaimer that "the effort required to *exhaust* a genus" is not "dispositive" is at odds with its *holding*—that Amgen's patents are not enabled because "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments." Pet. App. 14a (emphasis added). Regardless, it is clear that enablement of genus claims now depends not on the experimentation required to "make and use" "the invention," 35 U.S.C. § 112(a), but on the *cumulative* effort required to make and use some large range of embodiments. Now

patents are not enabled if the Federal Circuit subjectively decides there are "too many" embodiments to all be made and tested easily. But the Patent Act requires patentees to provide "some practicable way of putting [the invention] into operation." *The Telephone Cases*, 126 U.S. at 536. It does not demand claims so narrow that skilled artisans could make all (or most) embodiments in succession without "'substantial time and effort.'"

The Federal Circuit suggested that its rule prevents patentees from claiming more than they invented through claims that are "far broader in functional diversity than" the examples the patents disclose. 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 Federal Circuit's test is not necessary to address that concern. If a claim truly exceeds what the patent enables, the challenger will be able to provide "concrete identification" of at least *some* actual embodiment that cannot be made or used without "undue experimentation." *McRO*, 959 F.3d at 1100. Here, Sanofi-Regeneron identified *no* actual embodiment—no antibody within the claims—that could not be generated using the patents' disclosures. Pet. C.A. Br. 59; Pet. C.A. Reply 14-15.

The Federal Circuit has expressed concern about patents that leave skilled artisans "searching for a needle in a haystack to determine which," of a potentially huge number of "candidates," perform the claimed function. *Idenix*, 941 F.3d at 1162; see Pet. App. 15a. Patents, of course, cannot serve merely as "a starting point for further iterative research" on how to achieve a result. *Wyeth*, 720 F.3d at 1386. Claims thus may not be enabled when the "number of inoperative combinations" covered by a claim "becomes significant." *Atlas Powder Co.* v. *E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984).

They cannot consign skilled artisans to "synthesizing and screening" large numbers of "candidate" embodiments to find *any* that work. *Idenix*, 941 F.3d at 1163. But no specialized sub-test is required to address that concern. Such claims would not be enabled under this Court's standard, because a specification that effectively sends skilled artisans on a research mission 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. But again, that was not the case here—the jury heard testimony that Amgen's roadmap generates antibodies within the claims *every time*. See p. 10, *supra*.

The Federal Circuit's reach-the-full-scope test is a court-made solution to a non-existent problem. This Court has repeatedly overturned the Federal Circuit's efforts to supplant commonsense statutory standards with specialized tests of its own devising. See, *e.g.*, *Nautilus, Inc.* v. *Biosig Instruments, Inc.*, 572 U.S. 898, 901, 910 (2014) ("'insolubly ambiguous'" test for indefiniteness); *KSR Int'l Co.* v. *Teleflex Inc.*, 550 U.S. 398, 415, 419 (2007) ("teaching, suggestion, or motivation" test for obviousness). Review is warranted once again.

B. The Issue Is Exceptionally Important

The Federal Circuit's reach-the-full-scope requirement has profound impacts on innovation, particularly for pharmaceuticals and biotech. Its results are grossly unfair.

1. In the pharmaceutical and biotech industries, significant breakthroughs often involve identifying the mechanism for producing a desired effect and making a working embodiment. That mechanism, however, may have the same effect when implemented in any number of structurally similar compounds. "The central feature of patent law" in those fields thus "is the genus claim"—patent claims "that use functional language or generic formulas

to cover embodiments of the invention (species) that share a common attribute or property." *KLS*, *supra*, at 1, 15. Such claims are essential to offering patent protection commensurate with the invention's scope. Drawing claims to cover only particular embodiments does not provide "patent protection on the fruits of [the inventor's] investments." Pet. App. 65a. Copyists could "avoid infringement" 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). And requiring inventors to obtain a patent on every individual variation of a genus would be impractical and wasteful.

While the Federal Circuit has conceded that its standard imposes "high hurdles in fulfilling the enablement requirement," Pet. App. 12a, the reality is worse—it appears "impossible" to satisfy any time a genus claim covers a "nontrivial" number of embodiments, *KLS*, *supra*, at 4. As Judge Bryson noted, "[s]uch a rule would invalidate all broad claims for lack of enablement." *Erfindergemeinschaft UroPep GbR* v. *Eli Lilly & Co.*, 276 F. Supp. 3d 629, 661 (E.D. Tex. 2017), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018).

The Federal Circuit's enablement standard for genus claims has already had severe consequences, particularly for pharmaceuticals and biotechnology, as numerous commentators have recognized. See, *e.g.*, D. Kass, *Biologics Face Tougher Patent Scrutiny After Amgen Ruling*, Law360 (Feb. 18, 2021), https://bit.ly/2Q5fvKM; E. Silverman, *A U.S. Court Ruling May Force Biologics Makers To Review Patent Protections*, Stat+ (Feb. 25, 2021), https://bit.ly/3uzmzhD; A. Houldsworth, *The CAFC's* Amgen v. Sanofi *Decision Spells Trouble for Broad Functional Patent Claims*, iam (Feb. 16, 2021), https://bit.ly/3tf5k4Q; D. Crouch, *Functional Claim "Raises the Bar*

for Enablement," PatentlyO (Feb. 16, 2021), https://bit.ly/3tf5skQ. But any genus claim, in any field, is at risk of invalidation if it covers more than the disclosed embodiments. 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).

2. 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" sufficiently "that others may construct and use it." *Schriber-Schroth*, 305 U.S. at 57. The Federal Circuit's reach-the-full-scope standard reneges on the terms of that bargain.

To the Federal Circuit, it does not matter that the inventor created a groundbreaking innovation that reflects the very "progress" in "science and useful arts" patents are intended "[t]o promote." U.S. Const. art. I, §8, cl. 8. Nor does it matter that the inventor taught the world *exactly* how to "make and use" that invention. 35 U.S.C. §112(a). The Federal Circuit will invalidate the inventor's patent if it can speculate that too much time and effort might be required to identify "enough" variations, or that some theoretical variation lurking in hypothetical "*far corners* of the claimed landscape" might be "particularly inaccessible or uncertain." Pet. App. 65a (emphasis added).

That is not what §112 demands. And it is unfair in the extreme. Inventors with groundbreaking innovations should not be denied patent rights based on speculation about embodiments that might (or might not) exist in the

patent's extreme "corners"—or because the inventor has not undertaken the "obviously impossible" task of specifying every potential embodiment. *Minerals Separation*, 242 U.S. at 271. While the Federal Circuit purports to adhere to a standard of "reasonable enablement," Pet. App. 8a, its reach-the-full-scope test is the opposite.

III. THIS CASE IS AN IDEAL VEHICLE

This case presents an ideal vehicle. It squarely—and starkly—presents both questions.

Two separate juries found Amgen's claims enabled. By deeming enablement "a question of law" reviewed "without deference," Pet. App. 6a, the Federal Circuit overturned the verdict without attempting to meet the demanding standard for overturning jury factfindings. *Nat'l Commc'ns Ass'n* v. *AT&T Corp.*, 238 F.3d 124, 127 (2d Cir. 2001) ("high bar"); see 9B Wright & Miller, *Fed. Prac. & Proc. Civ.* §2524 (3d ed.). That burden was especially daunting here. "[G]ranting a judgment as a matter of law for the party bearing the burden of proof is reserved for extreme cases." 9B Wright & Miller, *supra*, §2535. Here, Sanofi-Regeneron bore a burden of proof by *clear-and-convincing* evidence. Yet, under the rubric of resolving a question of "law," the court resolved the issue contrary to two juries' findings.

Applying §112 as written, moreover, would have required the Federal Circuit to reinstate the jury's verdict. There was no dispute the patents' specification enabled a "person skilled in the art * * * to make and use" the claimed antibodies. 35 U.S.C. §112(a). Skilled artisans could readily make the 26 antibodies Amgen's patents disclosed by amino-acid sequence. See, *e.g.*, C.A. App. 51-116 (Figs. 2A-3JJJ), 240 (85:9-43), 3868 (598:21-23). It was undisputed that, by following the patents' roadmap, skilled artisans would generate antibodies within the claims *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 claimed antibodies "'quickly, efficiently, and cheaply,'" Pet. App. 42a. Amgen's expert specifically testified that the roadmap produces the full scope of claimed antibodies. C.A. App. 3908 (757:12-14), 3909 (762:14-20).

Neither the Federal Circuit nor Sanofi-Regeneron identified *any* actual embodiment that could not be made following the patents' teachings. But the Federal Circuit ruled there were "millions of candidates" for antibodies that *might* fall within the claims' far corners. Pet. App. 15a. It then invalidated the patents because, it believed, "'substantial time and effort' would be required *to reach the full scope* of claimed embodiments." Pet. App. 14a (emphasis added). That standard improperly "raises the bar for enablement." Pet. App. 13a. It is not what § 112 requires.

CONCLUSION

The petition should be granted.

Respectfully submitted.

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NOVEMBER 2021

APPENDIX

APPENDIX A
UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2020-1074

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,

Plaintiffs-Appellants,

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,

Defendants-Appellants.

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews

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Decided: February 11, 2021

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Before PROST, *Chief Judge*, LOURIE and HUGHES, *Circuit Judges*.

LOURIE, *Circuit Judge*.

Amgen Inc., Amgen Manufacturing, Ltd., and Amgen USA, Inc. (collectively, "Amgen") appeal from a decision of the United States District Court for the District of Delaware granting Judgment as a Matter of Law ("JMOL") of lack of enablement of claims 19 and 29 of U.S. Patent 8,829,165 (the "'165 patent") and claim 7 of U.S. Patent 8,859,741 (the "'741 patent"). See *Amgen Inc.* v. *Sanofi*, No. CV 14-1317-RGA, 2019 WL 4058927, at *1-2, *13 (D. Del. Aug. 28, 2019) ("Decision"). For the reasons set forth below, we affirm.

BACKGROUND

Elevated low-density lipoprotein ("LDL") cholesterol is linked to heart disease. LDL receptors remove LDL cholesterol from the blood stream, thus regulating the amount of circulating LDL cholesterol. The proprotein convertase subtilisin/kexin type 9 ("PCSK9") enzyme regulates LDL receptor degradation. PCSK9 binds to LDL receptors and mediates their degradation, thus decreasing the number of LDL receptors on a cell's surface. Antibodies may bind to and block PCSK9, allowing LDL receptors to continue regulating the amount of circulating LDL cholesterol.

Amgen owns the '165 and '741 patents, which describe antibodies that purportedly bind to the PCSK9 protein and lower LDL levels by blocking PCSK9 from binding to LDL receptors. The '165 and '741 patents share a common written description. See Appellants' Br. 10 n.2.

The specification discloses amino acid sequences for twenty-six antibodies, including the antibody (designated as "21B12") with the generic name of evolocumab, marketed by Amgen as Repatha®. See '165 patent col. 85 ll. 1-43; Appellants' Br. 11 n.3. As shown for example in Figure 20A of the '165 patent, the specification discloses three-dimensional structures for the antibodies designated 21B12 and 31H4 and shows where those antibodies bind to PCSK9. The '165 and '741 patents claim antibodies that bind to one or more of fifteen amino acids (*i.e.*, "residues") of the PCSK9 protein and block PCSK9 from binding to LDL receptors.

The relevant '165 patent claims are:

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.
>
> 29. A pharmaceutical composition comprising an isolated monoclonal antibody, wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO: 3 and blocks the binding of PCSK9 to LDLR by at least 80%.

'165 patent col. 427 l. 47-col. 430 l. 23.

> The relevant '741 patent claims are:
>
> 1. An isolated monoclonal antibody that binds to PCSK9, wherein the isolated monoclonal antibody binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
>
> 2. The isolated monoclonal antibody of claim 1, wherein the isolated monoclonal antibody is a neutralizing antibody.
>
> 7. The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.

'741 patent col. 427 ll. 36-57. The claimed antibodies are defined by their function: binding to a combination[ ] of sites (residues) on the PCSK9 protein, in a range from one residue to all of them; and blocking the PCSK9/LDLR interaction.

This is the second time that these patents have been on appeal in our court. Amgen filed suit against Sanofi, Aventisub LLC, Regeneron Pharmaceuticals Inc., and Sanofi-Aventis U.S. LLC (collectively, "Sanofi") on October 17, 2014, alleging infringement of multiple U.S. patents, including the '165 and '741 patents. *Decision* at *1. Amgen and Sanofi stipulated to infringement of selected claims (including '165 patent claims 19 and 29 and '741 patent claim 7) and tried issues of validity to a jury in March 2016. *Id.* During the trial, the district court granted JMOL of nonobviousness and of no willful infringement. *Id.* At the close of the trial, the jury determined that the patents were not shown to be invalid for lack of enablement and written description. *Id.*

Sanofi appealed to this court. Relevant to the current appeal, we held that the district court erred in its evidentiary rulings and jury instructions regarding Sanofi's defenses that the patents lack written description and enablement, and we remanded for a new trial on those issues. *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1381-82 (Fed. Cir. 2017). We also vacated the permanent injunction. *Id.*

On remand, the parties tried the issues of written description and enablement to the jury. The jury again found that Sanofi failed to prove that the asserted claims were invalid for lack of written description and enablement. Sanofi moved for JMOL and, in the alternative, for a new trial. *Decision* at *1; J.A. 895. The district court granted Sanofi's Motion for JMOL for lack of enablement and denied the motion for lack of written description. See *Decision* at *17; J.A. 35. The court also conditionally denied Sanofi's motion for a new trial. *Id.* Amgen timely appealed, and we have jurisdiction pursuant to 28 U.S.C. §1295(a)(1). See J.A. 909-10.

DISCUSSION

Whether a claim satisfies the enablement requirement of 35 U.S.C. §112 is a question of law that we review without deference, although the determination may be based on underlying factual findings, which we review for clear error. See *Alcon Research Ltd.* v. *Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014). The statutory basis for the enablement requirement is found in Section 112 of the patent statute, which provides in relevant part that a patent's specification must "enable any person skilled in the art . . . to make and use" the patented invention. 35 U.S.C. §112(a). The purpose of the enablement requirement is to ensure that the public is told how to carry out the invention, *i.e.*, to make and use it. We have held that

such disclosure must be "at least commensurate with the scope of the claims." *Crown Operations Int'l* v. *Solutia Inc.*, 289 F.3d at 1367, 1378-79 (Fed. Cir. 2002) (citing *Nat'l Recovery Techs., Inc.* v. *Magnetic Separation Sys.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999)).

"To prove that a claim is invalid for lack of enablement, a challenger must show by 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.'" *Alcon Research*, 745 F.3d at 1188 (quoting *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988)). "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *Wands*, 858 F.2d at 737. Those factual considerations, which have come to be known as the "*Wands* factors," are:

> (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.

As we have stated elsewhere, "[a]fter the challenger has put forward evidence that some experimentation is needed to practice the patented claim, the factors set forth in *Wands* then provide the factual considerations that a court may consider when determining whether the amount of that experimentation is either 'undue' or sufficiently routine such that an ordinarily skilled artisan would reasonably be expected to carry it out." *Alcon Research*, 745 F.3d at 1188 (quoting *Wands*, 858 F.2d at

737). Although a specification does not need to "describe how to make and use every possible variant of the claimed invention, when a range is claimed, there must be reasonable enablement of the scope of the range." *McRO, Inc.* v. *Bandai Namco Games Am. Inc.*, 959 F.3d 1091, 1100 (Fed. Cir. 2020) (citing *AK Steel Corp.* v. *Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)) (internal citations omitted).

On appeal, Amgen asks us to reverse the district court's decision holding '165 patent claims 19 and 29 and '741 patent claim 7 invalid for lack of enablement. Amgen contends that, under a proper analysis of the *Wands* factors, the claims at issue were enabled because no undue experimentation is required to obtain antibodies fully within the scope of the claims. Amgen points to expert testimony purportedly showing that a person of skill in the art can make all antibodies within the scope of the claims by following a roadmap using anchor antibodies and well-known screening techniques as described in the specification or by making conservative amino acid substitutions in the twenty-six examples. Amgen argues that the court erred by focusing on the effort required to discover and make every embodiment of the claims, see Appellants' Br. 32 (citing *Decision* at *7), while failing to recognize that Sanofi could not identify any antibody that cannot be made by following the specification's teachings. See Reply Br. 4-5; see also *McRO*, 959 F.3d at 1104 ("[A] usual requirement [is] that the challenger identify specifics that are or may be within the claim but are not enabled."). Amgen contends that the embodiments in the patent are structurally representative for the purpose of fulfilling the written description requirement, and such evidence is sufficient to indicate a structure/function correlation establishing enablement. See Reply Br. 23-24.

Sanofi responds that the district court properly concluded based on the *Wands* factors that the claims are not enabled because they require undue experimentation. As support for its position, Sanofi contends that there are millions of antibody candidates within the scope of the claims, the disclosures do not provide sufficient guidance, antibody generation is unpredictable, and practicing the full scope of the claims requires substantial trial and error. See Appellees' Br. 17-18, 56. According to Sanofi, the functionally defined claims cover a vast scope. See *id.* at 34-41. Sanofi argues that Amgen focused on "the number of antibodies actually known to satisfy the claims, when this court's precedents require examining the number of candidates that must be made and tested to determine whether they satisfy the claimed function." *Id.* at 18.

We begin by considering the *Wands* case itself, which has become the "go to" precedent for guidance on enablement, and which also involved claims relating to antibody technology. The broadest claim in *Wands* "involve[d] immunoassay methods for the detection of hepatitis B surface antigen by using high-affinity monoclonal antibodies of the IgM isotype." *Wands*, 858 F.2d at 733. The U.S. Patent and Trademark Office Board of Patent Appeals and Interferences had found that undue experimentation would be required for one skilled in the art to make the claimed antibodies used in the methods because "production of high-affinity IgM anti-HBsAg antibodies [was] unpredictable and unreliable." *Id.* at 735. We found, reviewing the facts, that the disclosure adequately taught using hybridoma technology to produce the needed claimed antibodies. See *id.* at 734. We stated that "no evidence was presented by either party on how many hybridomas would be viewed by those in the art as requir-

ing undue experimentation to screen," *id.* at 740, and we accordingly held that the specification fully enabled the claimed invention, see *id.* at 736.

Importantly, although *Wands* gave birth to its eponymous factors, *Wands* did not proclaim that all broad claims to antibodies are necessarily enabled. Facts control and, in this court, so does the standard of review. In considering the *Wands* factors, the district court compared the present case to other cases in which we found lack of enablement due to the undue experimentation required to make and use the full scope of the claimed compounds that require a particular structure and functionality. For example, in *Wyeth & Cordis Corp.* v. *Abbott Laboratories*, we held that claims covering methods of preventing restenosis with compounds having certain functionality requirements were invalid for lack of enablement. See 720 F.3d 1380, 1385-86 (Fed. Cir. 2013). Of particular significance, we held that due to the large number of possible candidates within the scope of the claims and the specification's corresponding lack of structural guidance, it would have required undue experimentation to synthesize and screen each candidate to determine which compounds in the claimed class exhibited the claimed functionality. *Id.*

Similarly, in *Enzo Life Sciences, Inc.* v. *Roche Molecular Systems, Inc.*, we found that the claims were similar to those at issue in *Wyeth* in that they required both a particular structure and functionality, and we held that the specification failed to teach one of skill in the art whether the many embodiments of the broad claims would exhibit that required functionality. See 928 F.3d 1340, 1345-48 (Fed. Cir. 2019). And, in *Idenix Pharmaceuticals LLC* v. *Gilead Sciences Inc.*, we affirmed the district court's determination that the claims had both

structural and functional limitations, and that undue experimentation would have been required to synthesize and screen the billions of possible compounds because, given a lack of guidance across that full scope, finding functional compounds would be akin to finding a "needle in a haystack." 941 F.3d 1149, 1160-63, 1165 (Fed. Cir. 2019); see *Idenix Pharms. LLC* v. *Gilead Scis., Inc.*, 2018 WL 922125 (D. Del. Feb. 16, 2018). The district court found that *Wyeth*, *Enzo*, and *Idenix* all support its conclusion that the asserted claims lack enablement. See *Decision* at *9-13.

What emerges from our case law is that the enablement inquiry for claims that include functional requirements can be particularly focused on the breadth of those requirements, especially where predictability and guidance fall short. In particular, it is important to consider the quantity of experimentation that would be required to make and use, not only the limited number of embodiments that the patent discloses, but also the full scope of the claim. As we recently explained:

> [C]onducting the *Wands* analysis has routinely involved concrete identification of at least some embodiment or embodiments asserted not to be enabled—including what particular products or processes are or may be within the claim, so that breadth is shown concretely and not just as an abstract possibility, and how much experimentation a skilled artisan would have to undertake to make and use those products or processes.

McRO, 959 F.3d at 1100. We then elaborated in a footnote that:

> In cases involving claims that state certain structural requirements and also require performance of some function (*e.g.*, efficacy for a certain purpose),

> we have explained that undue experimentation can include undue experimentation in identifying, from among the many concretely identified compounds that meet the structural requirements, the compounds that satisfy the functional requirement.

Id. at 1100 n.2 (citations omitted).

That reasoning applies here. While functional claim limitations are not necessarily precluded in claims that meet the enablement requirement, such limitations pose high hurdles in fulfilling the enablement requirement for claims with broad functional language. See, *e.g.*, *Wyeth*, 720 F.3d at 1384 (finding that practicing the full scope of the claims would require excessive experimentation); *Enzo*, 928 F.3d at 1345 (finding that the specification failed to teach whether the many embodiments would be both hybridizable and detectable upon hybridization); *Idenix*, 941 F.3d at 1155-56 (finding that the broad functional limitation of having efficacy against hepatitis C virus increased the number of nucleoside candidates that would need to be screened).

Each appealed claim in this case is a composition claim defined, not by structure, but by meeting functional limitations. We agree with the district court's finding that the specification here did not enable preparation of the full scope of these double-function claims without undue experimentation. See *Decision* at *13. The binding limitation is itself enough here to require undue experimentation.

Turning to the specific *Wands* factors, we agree with the district court that the scope of the claims is broad. While in and of itself this does not close the analysis, the district court properly considered that these claims were indisputably broad. The parties dispute the exact number of embodiments falling within the claims. However,

we are not concerned simply with the number of embodiments but also with their functional breadth. Regardless of the exact number of embodiments, it is clear that the claims are far broader in functional diversity than the disclosed examples.[1] If the genus is analogized to a plot of land, the disclosed species and guidance "only abide in a corner of the genus." *AbbVie Deutschland GmbH & Co.* v. *Janssen Biotech, Inc.*, 759 F.3d 1285, 1299-300 (Fed. Cir. 2014). Further, the use of broad functional claim limitations raises the bar for enablement, a bar that the district court found was not met.

We also agree with the district court that this invention is in an unpredictable field of science with respect to satisfying the full scope of the functional limitations. One of Amgen's expert witnesses admitted that translating an antibody's amino acid "sequence into a known three-dimensional structure is still not possible." J.A. 3910; see also *Decision* at *9. Another of Amgen's experts conceded that "substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be required to ensure that a substitution does not alter the binding and blocking functions." J.A. 3891; see also *Decision* at *9. And while some need for testing by itself might not indicate a lack of enablement, we note here the conspicuous absence of nonconclusory evidence that the full scope of the broad claims can predictably be generated by the described methods. Instead, we have evidence only that a small subset of examples of antibodies can predictably be generated.

---

[1] For example, there are three claimed residues to which not one disclosed example binds. See J.A. 4283; Appellees' Br. 52. And although the claims include antibodies that bind up to sixteen residues, none of Amgen's examples binds more than nine. See *id.*

Although the specification provides some guidance, including data regarding certain embodiments, we agree with the district court that "[a]fter considering the disclosed roadmap in light of the unpredictability of the art, any reasonable factfinder would conclude that the patent does not provide significant guidance or direction to a person of ordinary skill in the art for the full scope of the claims." *Decision* at *11. Here, even assuming that the patent's "roadmap" provided guidance for making antibodies with binding properties similar to those of the working examples, no reasonable factfinder could conclude that there was adequate guidance beyond the narrow scope of the working examples that the patent's "roadmap" produced.

As the district court noted, the only ways for a person of ordinary skill to discover undisclosed claimed embodiments would be through either "trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties," or else "by discovering the antibodies *de novo*" according to a randomization-and-screening "roadmap." *Id.* Either way, we agree with the district court that the required experimentation "would take a substantial amount of time and effort." *Id.* at *12. We do not hold that the effort required to exhaust a genus is dispositive. It is appropriate, however, to look at the amount of effort needed to obtain embodiments outside the scope of the disclosed examples and guidance. The functional limitations here are broad, the disclosed examples and guidance are narrow, and no reasonable jury could conclude under these facts that anything but "substantial time and effort" would be required to reach the full scope of claimed embodiments.

We therefore conclude that, after weighing the *Wands* factors, the court did not err in concluding that undue experimentation would be required to practice the full scope of these claims.

Finally, Amgen is incorrect that the district court's decision is inconsistent with *Wands* or that our affirmance here would overrule *Wands*. *Wands*, as indicated above, does not hold that antibody screening never requires undue experimentation. The holding in *Wands* was based on the facts of that case and the evidence presented there. Here, the evidence showed that the scope of the claims encompasses millions of candidates claimed with respect to multiple specific functions, and that it would be necessary to first generate and then screen each candidate antibody to determine whether it meets the double-function claim limitations. See *Decision* at *7-13. The facts of this case are thus more analogous to those in *Enzo*, *Wyeth*, and *Idenix*, where we concluded a lack of enablement.

CONCLUSION

We have considered Amgen's remaining arguments but find them unpersuasive. For the reasons above, we affirm the district court's determination that the asserted claims are invalid for lack of enablement.

AFFIRMED

APPENDIX B

IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

CIVIL ACTION NO. 14-1317-RGA

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AND AMGEN USA INC.,

Plaintiffs,

v.

SANOFI; SANOFI-AVENTIS U.S. LLC, AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., AND REGENERON PHARMACEUTICALS, INC.,

Defendants.

MEMORANDUM OPINION

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August 28, 2019

/s/ Richard G. Andrews
ANDREWS, U.S. DISTRICT JUDGE:

Currently pending before the Court are Defendants' Renewed Motion for Judgment as a Matter of Law ("JMOL") that the Asserted Patent Claims are Invalid and, in the alternative, Motion For a New Trial.[1] (D.I. 883, 886). I have reviewed the briefing for these motions. (D.I. 885, 888, 922, 923, 982, 983). I heard helpful oral argument on August 8, 2019. (Hr'g Tr.). The Parties submitted supplemental letters after argument. (D.I. 1045, 1046).

I. BACKGROUND

Plaintiffs Amgen, Inc., Amgen Manufacturing, Ltd., and Amgen USA Inc. filed suit against Defendants Sanofi, Sanofi-Aventis U.S. LLC, Aventisub LLC, and Regeneron Pharmaceuticals, Inc. on October 17, 2014 alleging

[1] Plaintiffs' Motion for a Permanent Injunction is also pending. (D.I. 870).

infringement of U.S. Patent Nos. 8,583,698 ("the '698 patent"), 8,829,165 ("the '165 patent"), and 8,859,741 ("the '741 patent"). (D.I. 1, 10, 184). Plaintiffs later amended the Complaint to add claims of infringement of U.S. Patent Nos. 8,871 ,913 ("the '913 patent"), 8,871,914 ("the '914 patent"), 8,883,983 ("the '983 patent"), and 8,889,834 ("the '834 patent"). (D.I. 184). The parties stipulated to infringement of selected claims for trial,[2] (D.I. 235), and tried issues of validity to the jury in March 2016. During trial, the Court granted JMOL of non-obviousness and no willful infringement. (D.I. 345 at 1076:6-1077:6; D.I. 302). The issue of damages was not tried to the jury. (D.I. 346 at 1285:16-20). The jury determined the patents were valid. (D.I. 303). Plaintiffs moved for a permanent injunction (D.I. 306), which was granted (D.I. 392), and then stayed. (D.I. 401). Defendants appealed. (D.I. 402).

On appeal, the Federal Circuit affirmed the grant of Plaintiffs' JMOL of non-obviousness and the denial of Defendants' JMOL of no written description and enablement but reversed for errors made in evidentiary rulings and jury instructions and remanded the case for a new trial on written description and enablement. *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1381-82 (Fed. Cir. 2017). The Federal Circuit also vacated the permanent injunction. *Id.*

On remand, the Parties tried the issues of written description and enablement to the jury.[3] The jury verdict found claim 7 of the '741 patent and claims 19 and 29 of the '165 patent valid, but invalidated claims 7 and 15 of the '165

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[2] The selected claims for the first trial were claims 2, 7, 9, 15, 19, and 29 of the '165 patent, claim 7 of the '741 patent, and claim 24 of the '914 patent. (D.I. 235).

[3] Plaintiffs further narrowed the claims for the remand trial to claims 7, 15, 19, and 29 of the '165 patent and claim 7 of the '741 patent. (D.I. 759; D.I. 768).

patent for lack of written description. (D.I. 817). Defendants now ask that the Court overturn the jury verdict under Federal Rule of Civil Procedure 50(b) or grant a new trial under Rule 59. (D.I. 883, 886).

> 1. An isolated monoclonal antibody, wherein, when bound to PCSK9, the monoclonal antibody binds to at least one of the following residues: S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of SEQ ID NO:3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.
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> **19. The isolated monoclonal antibody of claim 1 wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3.**
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> **29. A pharmaceutical composition comprising an isolated monoclonal antibody, wherein the isolated monoclonal antibody binds to at least two of the following residues S153, I154, P155, R194, D238, A239, I369, S372, D374, C375, T377, C378, F379, V380, or S381 of PCSK9 listed in SEQ ID NO:3 and blocks the binding of PCSK9 to LDLR by at least 80%.**

('165 patent, cls. 1, 19, 29 (disputed claims bolded)). The claim of the '741 patent still in dispute reads as follows:

> 1. An isolated monoclonal antibody that binds to PCSK9, wherein the isolated monoclonal antibody binds an epitope on PCSK9 comprising at least one of residues 237 or 238 of SEQ ID NO: 3, and wherein the monoclonal antibody blocks binding of PCSK9 to LDLR.

2. The isolated monoclonal antibody of claim 1, wherein the isolated monoclonal antibody is a neutralizing antibody.

7. The isolated monoclonal antibody of claim 2, wherein the epitope is a functional epitope.

('741 patent, cls. 1-2, 7 (disputed claim bolded)).

II. LEGAL STANDARD

A. JUDGMENT AS A MATTER OF LAW

Judgment as a matter of law is appropriate if "the court finds that a reasonable jury would not have a legally sufficient evidentiary basis to find for [a] party" on an issue. Fed. R. Civ. P. 50(a)(1). "Entry of judgment as a matter of law is a 'sparingly' invoked remedy, granted only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Marra* v. *Phila. Hous. Auth.*, 497 F.3d 286, 300 (3d Cir. 2007) (cleaned up).

"To prevail on a renewed motion for JMOL following a jury trial, a party must show that the jury's findings, presumed or express, are not supported by substantial evidence or, if they were, that the legal conclusion(s) implied [by] the jury's verdict cannot in law be supported by those findings." *Pannu* v. *Iolab Corp.*, 155 F.3d 1344, 1348 (Fed. Cir. 1998) (alterations in original). "'Substantial' evidence is such relevant evidence from the record taken as a whole as might be accepted by a reasonable mind as adequate to support the finding under review." *Perkin-Elmer Corp.* v. *Computervision Corp.*, 732 F.2d 888, 893 (Fed. Cir. 1984).

In assessing the sufficiency of the evidence, the Court must give the non-moving party, "as [the] verdict winner, the benefit of all logical inferences that could be drawn

from the evidence presented, resolve all conflicts in the evidence in his favor and, in general, view the record in the light most favorable to him." *Williamson* v. *Consol. Rail Corp.,* 926 F.2d 1344, 1348 (3d Cir. 1991). The Court may "not determine the credibility of the witnesses [nor] substitute its choice for that of the jury between conflicting elements in the evidence." *Perkin-Elmer,* 732 F.2d at 893. Rather, the Court must determine whether the evidence supports the jury's verdict. See *Dawn Equip. Co.* v. *Ky. Farms Inc.,* 140 F.3d 1009, 1014 (Fed. Cir. 1998); *Gomez* v. *Allegheny Health Servs. Inc.,* 71 F.3d 1079, 1083 (3d Cir. 1995) (describing standard as "whether there is evidence upon which a reasonable jury could properly have found its verdict"); 9B Charles Alan Wright & Arthur R. Miller, *Federal Practice and Procedure* § 2524 (3d ed. 2008) ("The question is not whether there is literally no evidence supporting the party against whom the motion is directed but whether there is evidence upon which the jury might reasonably find a verdict for that party.").

Where the moving party bears the burden of proof, the Third Circuit applies a different standard. This standard "'requires the judge to test the body of evidence not for its insufficiency to support a finding, but rather for its overwhelming effect.'" *Fireman's Fund Ins. Co.* v. *Videfreeze Corp.*, 540 F.2d 1171, 1177 (3d Cir. 1976) (quoting *Mihalchak* v. *Am. Dredging Co.*, 266 F.2d 875, 877 (3d Cir. 1959)). The Court "'must be able to say not only that there is sufficient evidence to support the finding, even though other evidence could support as well a contrary finding, but additionally that there is insufficient evidence for permitting any different finding.'" *Id.* at 1177 (quoting *Mihalchak*, 266 F.2d at 877).

B. NEW TRIAL

Federal Rule of Civil Procedure 59(a)(1)(A) provides, in pertinent part: "The court may, on motion, grant a new trial on all or some of the issues—and to any party— . . . after a jury trial, for any reason for which a new trial has heretofore been granted in an action at law in federal court . . . ." Among the most common reasons for granting a new trial are: (1) the jury's verdict is against the clear weight of the evidence, and a new trial must be granted to prevent a miscarriage of justice; (2) newly discovered evidence exists that would likely alter the outcome of the trial; (3) improper conduct by an attorney or the court unfairly influenced the verdict; or (4) the jury's verdict was facially inconsistent. See *Zarow-Smith* v. *N.J. Transit Rail Operations, Inc.*, 953 F. Supp. 581, 584-85 (D.N.J. 1997).

The decision to grant or deny a new trial is committed to the sound discretion of the district court. See *Allied Chem. Corp.* v. *Daiflon, Inc.*, 449 U.S. 33, 36 (1980); *Olefins Trading, Inc.* v. *Han Yang Chem. Corp.*, 9 F.3d 282, 289 (3d Cir. 1993) (reviewing district court's grant or denial of new trial motion under the "abuse of discretion" standard). Although the standard for granting a new trial is less rigorous than the standard for granting judgment as a matter of law—in that the Court need not view the evidence in the light most favorable to the verdict winner—a new trial should only be granted where "a miscarriage of justice would result if the verdict were to stand," the verdict "cries out to be overturned," or where the verdict "shocks [the] conscience." *Williamson*, 926 F.2d at 1352-53.

III. DISCUSSION

A. JUDGMENT AS A MATTER OF LAW OF NO WRITTEN DESCRIPTION

Defendants argue that no reasonable jury could conclude that the claims are supported by written description under either the representative species test or the structural features test. (D.I. 888 at 4-5).

The written description requirement contained in 35 U.S.C. § 112, ¶ 1 requires that the specification "clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad Pharm., Inc.*, v. *Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (cleaned up). "In other words, the test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "This inquiry, as we have long held, is a question of fact. Thus, we have recognized that determining whether a patent complies with the written description requirement will necessarily vary depending on the context." *Ariad*, 598 F.3d at 1351 (internal citations omitted). For patents that claim a broad genus (a major class or kind of thing) while disclosing only species of that genus (subclasses), the written description requirement is more specific. There are two tests. They are the representative species test and the structural features test. The Federal Circuit has summarized their requirements as follows:

> Demonstrating possession "requires a precise definition" of the invention. To provide this "precise definition" for a claim to a genus, a patentee must disclose "a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of

> skill in the art can visualize or recognize the members of the genus."

Amgen, 872 F.3d at 1373 (quoting *Ariad*, 598 F.3d at 1350).

The representative species test does not require disclosure of every species in the genus and there is no bright-line rule "governing [ ] the number of species that must be disclosed to describe a genus claim, as this number necessarily changes with each invention, and it changes with progress in a field." *Ariad*, 598 F.3d at 1351. However, "merely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species." *Id.* at 1350. "One needs to show that . . . one has conceived and described sufficient representative species encompassing the breadth of the genus." *AbbVie*, 759 F.3d at 1300.

Under the structural features test, "[f]unctional claim language can meet the written description requirement when the art has established a correlation between structure and function," such that disclosure of the function implicitly discloses the common structural features of the genus. *Ariad*, 598 F.3d at 1350.

"A party must prove invalidity for lack of written description by clear and convincing evidence." *Vasudevan Software, Inc.* v. *MicroStrategy, Inc.*, 782 F.3d 671, 682 (Fed. Cir. 2015). Because lack of written description, "like any other ground of invalidity, must be established by clear and convincing evidence," Defendants' burden on a JMOL motion is "doubly high: it must show that no reasonable jury could have failed to conclude that [Defendants'] case had been established by clear and convincing evidence." *Boehringer Ingelheim Vetmedica, Inc.* v.

Schering-Plough Corp., 320 F.3d 1339, 1353 (Fed. Cir. 2003) (internal citation omitted).

I start with the representative species test. Defendants argue that to satisfy the representative species test in the antibody context, the patentee "must adequately describe representative antibodies to reflect the structural diversity of the claimed genus" and "describe some species representative of antibodies that are structurally similar to" infringing antibodies. *AbbVie*, 759 F.3d at 1301. Defendants argue that Plaintiffs have not satisfied the representative species test because the undisputed evidence at trial indicated that the amino acid sequences of the disclosed antibodies and the infringing Competitor Antibodies[4] were completely different from one another. (D.I. 888 at 6-7). Plaintiffs argue that there was substantial evidence submitted at trial supporting a jury finding that the disclosed antibodies were representative of the structural diversity of the genus, including the Competitor Antibodies. (D.I. 923 at 5-6).

I agree with Plaintiffs that substantial evidence supports the jury verdict under the representative species test. The record contains contradictory evidence on (1) what the appropriate comparison metric was, (2) whether there was sufficient similarity between the amino acid sequences of the Competitor Antibodies and the disclosed examples in the patents, and (3) whether there was functional similarity between the Competitor Antibodies and the disclosed examples in the patents.

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[4] I adopt the Parties' terminology from trial. The Competitor Antibodies are infringing antibodies developed by Plaintiffs' competitors, Merck, Pfizer, and Defendant. They are Praluent, 1D05, AX132, and J16. (D.I. 888 at 6).

First, Plaintiffs' experts repeatedly disputed the use of amino acid sequence as an appropriate comparison to determine whether the disclosed species were representative of the genus. (D.I. 865 at 638:8-11, 768:18-20, 765:10-766:12, 769:14-770:24). Plaintiffs' experts testified that three-dimensional structure was the appropriate metric for comparison and presented substantial evidence of similarity in the three-dimensional structure of the antibodies disclosed in the patent and the Competitor Antibodies.[5] (*Id.* at 621:5-629:1, 633:12-637:17, 764:6-767:15, 724:9-10, 725:21-727:4, 772: 154-775: 17; D.I. 864 at 449:5-9).

Second, even if amino acid sequence was the appropriate metric for comparison, substantial evidence supported a finding of structural similarity between the Amgen Antibodies and the Competitor Antibodies. The amino acid sequence differences between the Competitor Antibodies are not as extreme as in *AbbVie*. In *AbbVie*, the Court determined that "[a]ll of the antibodies described in AbbVie's patents were derived from Joe-9 and have VH3 type heavy chains and Lambda type light chains" and "the patents [did] not describe any example [ ] of fully human IL-12 antibodies having heavy and light chains other than the VH3 and Lambda types." *AbbVie*, 759 F.3d at 1300. Unlike there, here there was testimony of 80% similarity between the disclosed antibodies and the Competitor Antibodies' amino acid sequences, (D.I. 864 at 371:2-10, 374: 19-24), and the disclosed antibodies cover more classes of antibodies than the patent disclosed in *AbbVie*. (D.I. 865 at 771:3-11). Dr. Rees testified that there are eight differ-

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[5] Defendants argue that Plaintiffs were improperly permitted to enter into evidence post-priority-date evidence about the three-dimensional structure. As Defendants include this challenge in their Rule 59 Motion for a New Trial, I will address it there.

ent families of binding and blocking antibodies disclosed by the patents. (D.I. 865 at 771:3-11).

Third, Plaintiffs presented substantial evidence of functional similarity. There was significant testimony that the antibodies disclosed in the 2008 patent application, while binding to different residues[6] across the "sweet spot," blocked PCSK9 binding to LDL-R through a variety of binding interactions. (D.I. 864 at 471:24-372:6; D.I. 865 at 630:14-25, 649:10-650:1, 651:1-652:11).

The jury was entitled to credit the testimony of Plaintiffs' experts. Thus, substantial evidence in the record supports the jury verdict of validity under the representative species test.

Because satisfaction of the representative species test is sufficient to support a finding of validity under written description, I need not address the Common Structural Features Test. Defendants have failed to show "that no reasonable jury could have failed to conclude that [Defendants'] case [for lack of written description] had been established by clear and convincing evidence." *Boehringer*, 320 F.3d at 1353 (internal citation omitted). I will therefore deny Defendants' motion for JMOL on the issue of written description.

B. JUDGMENT AS A MATTER OF LAW OF NO ENABLEMENT

Defendants argue that no reasonable jury could conclude that the asserted claims were enabled. (D.I. 888 at 13-14). Defendants advance two arguments: (1) the claims are not enabled because the vast majority of antibodies within the full scope of the claims are impossible to make,

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[6] Residues are amino acids that make up the PCSK9 protein, and in the context of the patent, are within the "sweet spot" where PCSK9 would bind with an LDL receptor. (D.I. 863 at 194:22-196:1).

and (2) undue experimentation is required to make antibodies within the claimed genus. (*Id*. at 14). The Parties agreed at oral argument that the disputed claims rise and fall together for the purposes of enablement. (Hr'g Tr. at 6:16-18, 6:23-7:8).

The enablement requirement, considered a separate and distinct requirement contained in 35 U.S.C. § 112, ¶ 1, assesses whether "one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *Sitrick* v. *Dreamworks, LLC,* 516 F.3d 993, 999 (Fed. Cir. 2008). "To be enabling, 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 Corp.* v. *Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012) (internal quotation marks omitted; emphasis added). Because the enablement inquiry takes into account what is known to one skilled in the art, the Federal Circuit has "repeatedly explained that a patent applicant does not need to include in the specification that which is already known to and available to one of ordinary skill in the art." *Koito Mfg. Co.* v. *Turn-Key-Tech, LLC*, 381 F.3d 1142, 1156 (Fed. Cir. 2004). "Enablement is a legal question based on underlying factual determinations." *Vasudevan*, 782 F.3d at 684. On a motion for JMOL, I must defer to the jury's underlying factual determinations, *Williamson*, 926 F.3d at 1348, but review the legal question *de novo*. *Pannu*, 155 F.3d at 1348. Factors considered in assessing the enablement requirement include:

> (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.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). "A party must prove invalidity for lack of enablement by clear and convincing evidence." *Vasudevan*, 782 F.3d at 684. Because lack of enablement, "like any other ground of invalidity, must be established by clear and convincing evidence," Defendants' burden on a JMOL motion is "doubly high: it must show that no reasonable jury could have failed to conclude that [Defendants'] case had been established by clear and convincing evidence." *Boehringer*, 320 F.3d at 1353 (internal citation omitted).

To enable the "full scope" of the claims, it is not required that the specification "provide[s] a detailed recipe for preparing every conceivable permutation" of a claimed embodiment. *Pfizer Inc.* v. *Teva Pharm. USA, Inc.*, 555 F. App'x 961, 967 (Fed. Cir. 2014). Yet, merely enabling a person of ordinary skill to practice an embodiment, or even several embodiments, is not always sufficient. See, *e.g.*, *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013) (determining that the specification provided "only a starting point for further iterative research in an unpredictable and poorly understood field"); *MagSil*, 687 F.3d at 1382-83 (patent claims on "change in the resistance level by at least 10%" with no upper boundary were not enabled because specification did not explain any way to achieve levels above a certain threshold); *Sitrick*, 516 F.3d at 999-1001 (not enabled because the specification did not explain how to integrate "user image" in movies). Thus, "the full scope of a claim is not enabled when there is an embodiment within the claim's scope that a person of ordinary skill, reading the specification, would be unable to practice without undue experimentation."

MorphoSys AG v. *Janssen Biotech, Inc.*, 358 F. Supp. 3d 354, 368-69 (D. Del. 2019).

1. Impossibility

Defendants argue that "the vast majority of antibodies within the full scope of the claims are impossible to make" and thus, the claims are not enabled. (D.I. 888 at 14). Defendants assert that *Trustees of Boston University* v. *Everlight Electronics Co.*, 89 F.3d 1357 (Fed. Cir. 2018), controls the inquiry. In *Everlight*, the Federal Circuit held a patent claim invalid for lack of enablement where the experts agreed that one out of six permutations of the claim was "physically impossible." *Id.* at 1362. Plaintiffs disagree, arguing, "Defendants have provided no evidence that any embodiments that *satisfy [Plaintiffs']* Claims are impossible to make." (D.I. 923 at 19).

First, Defendants point to testimony elicited on cross-examination from Plaintiffs' witnesses about two hypothetical antibodies: (1) an antibody that binds to only two of the specified residues on opposite sides of the "sweet spot" without touching any of the other thirteen residues, and (2) an antibody binding only to D238 and no other claimed residues. (D.I. 864 at 540:7-21; D.I. 865 at 796:9-12). In regards to the first hypothetical antibody, Dr. Rees testified, "I won't say its impossible, but I don't believe based on good protein structural principle an antibody could bridge across without also interacting with those amino acids in between." (D.I. 865 at 796:23-797:1). In regards to the second hypothetical antibody, Dr. Jackson testified, "An antibody wouldn't bind if it's just binding with one amino acid residue, it wouldn't have the binding strength." (D.I. 864 at 540:19-21).

These statements do not support the "impossibility" theory Defendants advance. Dr. Rees' testimony does not state that it would be impossible to make the first hypo-

thetical embodiment, just unlikely. Dr. Jackson's testimony indicates that an antibody that binds to just one amino acid residue would not fall within the scope of the claims because it would not actually bind to PCKS9 or block the binding of PCKS9 to the LDL receptor. (See '741 patent, cl. 1-2, 7).

Second, Defendants' reliance on *Everlight* is unavailing. In *Everlight*, the claims were drafted to cover six enumerated permutations of the patented invention. *Everlight*, 896 F.3d at 1360, 1364. In contrast, here, Plaintiffs' patent claims are drafted to require both (1) binding to "at least" one or two specified residues and (2) blocking PCSK9 from binding to the LD L-R. ('741 patent, cl. 1-2, 7; '165 patent, cl. 1, 19, 29). This patent language does not claim a full scope of binding to only one or two specified residues and nothing more. Thus, *Everlight* does not require a determination of no enablement as a matter of law.

2. Undue Experimentation

Defendants argue that the *Wands* factors require a conclusion of non-enablement as a matter of law. (D.I. 888 at 15). The *Wands* factors are used to determine whether the amount of experimentation required to practice the claims' full scope is "undue." See *Alcon Research Ltd.* v. *Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014). As noted, the *Wands* factors are:

> (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.

858 F.2d at 737.

a. Breadth of the Claims

After careful review of the evidence, I conclude that a reasonable factfinder could only have found that the scope covered by the claims is broad. Plaintiffs[ ] rel[y] on Dr. Rees' testimony that "the genus . . . would be narrow," (See D.I. 923 at 4 (citing D.I. 865 at 725:4-5, 731:16-17, 732:7-8)), because an antibody scientist would not engage in random mutations to the disclosed antibodies. (D.I. 865 at 733:6-11). But this testimony does not aid in the inquiry of what the full scope is of the claims of the asserted patents. Except for product-by-process claims or product claims with a process limitation, the method by which the patented product is made has no effect on the scope of the product claim. *Abbott Labs.* v. *Sandoz*, 566 F.3d 1282, 1293 (Fed. Cir. 2009) (en banc). An antibody scientist's refusal to engage in random mutations does not mean that there could not be embodiments of the claims that could only be discovered by performing a random mutation. Dr. Rees did not testify that every antibody within the scope of the claims could be made through intelligent substitution, nor did he testify as to how many antibodies would result from making "intelligent substitutions," other than that it would not result in "millions" of antibodies. (*Id.* at 732:7-8). Dr. Rees' testimony that the genus is "narrow" falls short because it does not actually address the breadth of the claims; it is at most merely a conclusory statement that the claim scope is not as large as Defendants' expert testified it was. The quantity that Dr. Rees meant by "narrow" is unknown. Such conclusory expert testimony is insufficient to support a factual determination that the claimed genus is in fact "narrow."

Additionally, part of Dr. Rees' testimony relied on Dr. Jackson's testimony regarding the development stages of Plaintiffs' antibody project. Dr. Jackson testified that the

initial testing processes determined that 3,000 of the antibodies created from immunizing ten mice bound to PCSK9. (D.I. 864 at 351:12-15, 351:24-352:3). Further testing revealed that 384 antibodies blocked interaction of PCSK9 with the LDL receptor, and that 84 antibodies were strong blockers. (*Id.* at 352:4-17). Dr. Rees also testified that "if the millions of antibodies that Dr. Boyd described . . . continued [ ] to bind and block . . . they would [ ] fall within the claims." (D.I. 865 at 733:2-7). Thus, Dr. Rees tacitly admitted that the potential scope of the claims could be broader than just those generated by intelligent substitution.

Dr. Boyd testified that if a person of ordinary skill in the art only created new antibodies by substituting amino acids per Table 1 of the patents in the sequence of a single disclosed antibody, the person of ordinary skill would obtain 97,000 antibodies that she would then have to test to see whether they bound to PCKS9 and blocked binding to LDL receptors. (*Id.* at 802:12-23). After doing these substitutions for every disclosed antibody, Dr. Boyd testified that the person of ordinary skill in the art would get "millions" of antibodies. (*Id.*). Even assuming a majority of these millions of antibodies would not satisfy the claim requirements for blocking interaction between PCSK9 and the LDL receptor, there does not appear to be a genuine dispute between the parties as to the scope of antibodies that would need to be tested to determine whether they fell within the claims. (D.I. 865 at 740:18-21, 779:10-20). The Federal Circuit has repeatedly endorsed the consideration of the "number of possible candidates falling within the claimed genus" in the enablement inquiry. *Enzo Life Scis., Inc.* v. *Roche Molecular Sys., Inc.*, 928 F.3d 1340, 1346 (Fed. Cir. 2019); *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1385 (Fed. Cir. 2013) ("even if

potential rapamycin compounds must have a molecular weight below 1,200 Daltons, there are still at least tens of thousands of candidates"). That is, even if potential antibodies must block PCSK9 from binding to LDL receptors, there are still at least millions of candidates.[7] Plaintiffs have repeatedly asserted that a person of ordinary skill in the art would not make substitutions by rote substitution following Table 1 of the patent, but instead, use their knowledge to make a smaller subset of "intelligent substitutions." (Hr'g Tr. at 75:13-17, 98:23-99:10). However, Dr. Rees has never testified as to how a person of ordinary skill would determine what subset of substitutions from Table 1 should be made. (D.I. 865 at 733:12-15). Thus, there is not a genuine material dispute of fact as to the breadth of the claims, and a reasonable factfinder could only conclude on this factual record that the scope of the claims is vast.

b. Predictability of the Art

Defendants contend that the art was "highly unpredictable" as "even the most highly skilled person could not determine [where an antibody will bind] from its [amino acid sequence]." (D.I. 888 at 16). The Parties disagree as to how to assess this factor. Defendants argued that under *Enzo* and *Wyeth*, the question is, when looking at the input, which "in this case [is] an antibody, how predictable is it by looking at it that it will or won't meet the functional limitation." (Hr'g Tr. at 34:6-21). Plaintiffs argued that predictability should be assessed by looking at the maturity and relative skill of those in the art.[8] (Hr'g Tr. at

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[7] Per Dr. Boyd's calculations from just the substitutions suggested by the patent specification. See '165 patent, tbl. 1.

[8] Plaintiffs argued at oral argument that both *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), and *Johns Hopkins Univ* v. *CellPro*, *Inc.*, 152 F.3d 1342 (Fed. Cir. 1998), were cases finding patents enabled in the

69:3-6, 9-11, 20-24). However, the state of the art and the relative skill of those in the art are separately enumerated factors under the *Wands* test.[9]

There was conflicting testimony as to the predictability of the art at the time of the 2008 patent application. Dr. Boyd testified that the amino acid sequences for antibodies are generally unpredictable because the unpredictability best serves the immune system; in his words, "If the antibodies were always predictable then the viruses and bacteria could figure out a way to get around them." (D.I. 863 at 225:9-17). Dr. Mehlin of Amgen, one of the inventors, testified:

> in general conservative mutations are going to be better tolerated by a protein than nonconservative mutations. But I'm always surprised. I mean, I have been surprised in the past where sometimes what you think is a conservative mutation is not conservative at all, you know, in terms of the protein function . . . [T]he only way to know in the end is to test it,

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context of antibody technology decades earlier. (Hr'g Tr. at 65:5-23). However, the patent in *In re Wands* was a method patent, 858 F.2d at 734, and in *Hopkins*, the finding of enablement was based on Defendants' failure to raise a genuine issue of material fact. 152 F.3d at 1359-60. Similarly, Plaintiffs also cited to *Erfindergemeinschaft UroPep GbR* v. *Eli Lilly & Co.*, 276 F. Supp. 3d 629, 663 (E.D. Tex. 2017). However, as in *Wands*, the claim at issue was a method claim rather than a genus claim. *Id.* at 640-41.

[9] Similarly, Plaintiffs' brief groups together four of the *Wands* factors: nature of the invention, state of the art, relative skill of those in the art, and predictability of the art. (D.I. 923 at 15). However, the entirety of Plaintiffs' discussion on these factors is, "the level of skill in the art was high, the art was advanced, and the techniques involved in Amgen's roadmap were routine and well-known." (*Id.*). None of Plaintiffs' assertions address the predictability of the art.

> right. You can't tell a priori that your mutation will be tolerated.

(D.I. 864 at 388:21-389:8).

Dr. Rees testified that the art is "a highly predictable area" because of the maturity of the art and the disclosures in the patent. (D.I. 865 at 757:2-11). However, he also testified that "the way in which you get from sequence to the three-dimensional structure isn't fully understood today." (*Id.* at 765:15-16). Dr. Rees also admitted that a person of ordinary skill would not know the exact substitutions needed in the amino acid sequence to alter the residues of PCSK9 to which the antibody will bind.[10] (*Id.* at 792:12-20, 793:5-13, 794:6-16). Dr. Rees' assertion that the art is "highly predictable," even taken in the light most favorable to Plaintiffs, is thus a conclusory assertion inconsistent with the rest of his testimony. At best, Dr. Rees' testimony indicates that a person of ordinary skill in the art would understand that conservative substitution could be used to make different antibodies that had the same or improved binding to the antigen. (D.I. 865 at 733:14-22). However, this testimony does not support Plaintiffs' position that testing would not be necessary for conservative substitutions and the position is contradicted by other testimony in the record from Plaintiffs' other expert, Dr. Petsko. Dr. Petsko testified that substitutions in the amino acid sequence of an antibody can affect the antibody's function, and testing would be required to ensure that a substitution does not alter the binding and blocking functions. (D.I. 865 at 688:21-689:10).

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[10] There was no explicit testimony from Dr. Rees at trial that antibodies resulting from "intelligent substitutions" in known antibodies would not require testing to ensure that they had the binding and blocking functions required by the asserted claims.

Plaintiffs, at oral argument, attempted to distinguish this case from *Enzo*, *Idenix Pharms. LLC* v. *Gilead Scis., Inc.*, 2018 WL 922125 (D. Del. Feb. 16, 2018), and *Morphosys*, arguing that the evidence in this case displays a structure-function relationship that was absent in those cases. (Hr'g Tr. at 77:16-78:3; 85:22-24). Plaintiffs assert that expert testimony established "that all antibodies that bind to the sweet spot have common structures—both three-dimensional shape and chemical structural features—that allow them to bind there." (D.I. 923 at 11). The experts' testimony, as Plaintiffs tacitly admitted in their briefing, focused upon the "sweet spot" of the antigen and its "unique three dimensional and chemical structure" that conveys the "structural information (common shape and chemical complementarity) of the antibodies that bind to it." (*Id*). Defendants' experts hotly contested the existence of such a structure-function relationship for the purposes of written description. (D.I. 888 at 9-13).

In the enablement context, there is no testimony from any expert that the structure-function relationship would eliminate the need for testing newly-created antibodies to determine whether they had the functions of blocking and binding. The Federal Circuit has "concluded that instead of analogizing the antibody-antigen relationship to a 'key in a lock,' it was more apt to analogize it to a lock and 'a ring with a million keys on it.'" *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1377 (Fed. Cir. 2017) (cleaned up). Here, while the shape of the "key" or antibody may help narrow the number to be tested in the "lock" or antigen, the expert testimony offered by Plaintiffs is that how to make a "key" or antibody in the correct shape is not "fully understood" (D.I. 865 at 765:15-16), from which it follows that the structure-function relationship is unpredictable.

Therefore, a reasonable factfinder could only find that the art is unpredictable.

c. Nature of the Invention; State of the Prior Art; Relative Skill of Those in the Art

The evidence indicates that the methods disclosed in the patent for making the invention were routine and well-known in the prior art. (D.I. 864 at 347:9-12, 347:18-22, 348:16-24; D.I. 865 at 713:15-18). There does not appear to be any dispute between the parties that the techniques disclosed could conceivably allow a person of ordinary skill in the art to make at least some antibodies falling within the patent claims. Neither does there appear to be any dispute as to the level of skill in the art. A person of ordinary skill in the art would be familiar with the techniques disclosed in the patent: binning, alanine scanning, x-ray crystallography, immunizing mice, and making amino acid substitutions. (D.I. 864 at 347:9-12, 347:18-22, 348:16-24; D.I. 865 at 713:15-18).

d. Amount of Direction or Guidance Presented; Presence and Number of Working Examples

The record, taken in the light most favorable to Plaintiffs, indicates that there is no genuine dispute as to the amount of direction/guidance presented or the number of working examples present in the patent specifications.

Although the patent provides twenty-six working examples, the record indicates that there is no dispute that they do not teach a person of ordinary skill in the art how to predict from an antibody's sequence whether it will bind to specific PCKS9 residues. (D.I. 864 at 389:3-8; D.I. 865 at 779:10-14, 793:12-20, 794:11-16). Neither does the patent provide any direction or guidance on how to predict whether an antibody will bind. (D.I. 865 at 779:10-14,

794:11-16). Even for the suggested substitutions in the patent ('165 patent, table 1), a person of ordinary skill in the art would still be required to test the newly-generated antibody to see if it meets the functional limitations of the claims. (*Id.*). This is less guidance than was provided by the patent in *MorphoSys*, where the testimony indicated that "conservative variants of the disclosed [CD38] antibodies could be designed and would be 'reasonably expected' to be effective without screening." 358 F. Supp. 3d at 372.

The record also indicates that the specification and the examples do not improve a person of ordinary skill in the art's ability to discover non-disclosed antibodies within the scope of the claims. Plaintiffs' expert, Dr. Rees, using claim 7 of the '741 patent as an example, testified that the patent teaches the following roadmap:

> Step 1: Make a known antibody binding D238;
>
> Step 2: Generate a pool of antibodies through super immunization procedure and test the pool of antibodies to see if they bind to PCSK9;
>
> Step 3: Run a binning assay against the known antibody to identify competing antibodies;
>
> Step 4: Run a blocking assay to determine whether the antibodies block the binding of PCSK9 to the LDL receptor; and
>
> Step 5: Verify the identity of the amino acids bound by alanine or arginine scanning

(D.I. 865 at 737:17-738-10, 739:15-745:12). In comparison, the inventor, Dr. Jackson testified to the following methods ("the research plan") implemented in discovering the twenty-six disclosed antibodies:

> Step 1: Generate a pool of antibodies by super immunizing mice;

Step 2: Test the pool of antibodies to see if they bind to PCSK9;

Step 3: Test the pool of binders to determine whether and how much the antibodies block the binding of PCKS9 to the LDL receptor;

Step 4: Attempt to characterize through a competition/binning assay; and

Step 5: Generate amino acid sequences and identify the amino acid residues bound by the antibodies.

(D.I. 864 at 501:23-502:15, 503:7-504:9, 504:22-505:15, 507:1-508:23, 513:15-19). Dr. Jackson also testified that the patent describes "optimiz[ing]" the binding test by putting PCSK9 "in the right position so that [the binding] site was accessible to the antibodies." (*Id.* at 503:18-23). The significant similarity between the "research plan" used by Dr. Jackson and the "roadmap" disclosed in the patent demonstrates that a person of ordinary skill in the art attempting to obtain a claimed antibody that is not disclosed or is a variant of a disclosed antibody "would have to do essentially the same amount of work as the inventors of the patents-in-suit." *MorphoSys AG*, 358 F. Supp. 3d at 372; see also *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013) (invalidating patent for lack of enablement where specification "disclose[d] only a starting point for further iterative research in an unpredictable and poorly understood field."). As in *MorphoSys*, a person of ordinary skill in the art "would have to discover these [nonconservative variant] antibodies de novo through" super immunization or another technique. 358 F. Supp. 3d at 372. After considering the disclosed roadmap in light of the unpredictability of the art, any reasonable factfinder would conclude that the patent does not provide significant guidance or direction to a person of

ordinary skill in the art. A person of ordinary skill in the art can only discover undisclosed claimed embodiments either (1) through trial and error, by making changes to the disclosed antibodies and then screening those antibodies for the desired binding and blocking properties, or (2) by discovering the antibodies *de novo*.

e. The Quantity of Experimentation Necessary

Defendants argue,

> The quantity of experimentation required to make and use the full scope of the Claims is vast … [because] a skilled artisan must either (1) randomly generate pools of antibodies, or (2) make substitutions to known antibodies, [and then] test those resulting antibodies to determine whether they satisfy the functional limitation of binding to specified PCSK9 residues.

(D.I. 888 at 17). More specifically, Defendants argue that a person of ordinary skill in the art may not be able to make a desired antibody using the patent's specification. As noted above, there is no dispute between the parties that a person of ordinary skill in the art would need either to follow the roadmap to generate a pool of antibodies for further testing, or to make substitutions to known antibodies and then to test the newly created antibodies.

The parties dispute how much experimentation is needed. Defendants assert that because of the unpredictability of the art and the need for functional testing, the experimentation required is an "iterative trial and error" process that will take substantial time and effort. (D.I. 888 at 18; D.I. 864 at 329:2-13, 329:16-24). In fact, Dr. Boyd testified that a person of ordinary skill in the art might never know whether the entire claim scope had been discovered. (D.I. 864 at 330:18-22). Dr. Rees admitted that

generating large pools of antibodies was impractical. (D.I. 865 at 779:23-780:3; 781:10-14). Plaintiffs argue that the quantity of experimentation required to make the full scope of the claims is low and points to Dr. Rees' testimony that "automated high-throughput techniques existed for testing a large number of antibodies" to determine whether they fall within the scope of the claims "quickly, efficiently, and cheaply." (D.I. 923 at 15; D.I. 865 at 761:6-762:4). However, Dr. Rees' testimony about the time and effort required was largely conclusory. (D.I. 865 at 761:6-13). Such conclusory expert testimony is insufficient to support a factual conclusion that the time and effort required to enable the full scope of the claims is minimal. In contrast, Dr. Boyd testified that "you could be immunizing mice for a hundred years. There might be kind of an antibody that you didn't come up with in that time period and no one else came up with but it might be still out there waiting to be found . . ." (D.I. 864 at 330:18-22). Also, as noted above, the significant similarity between the "research plan" used by Dr. Jackson and the "roadmap" disclosed in the patent (as testified to by Dr. Rees) demonstrates that a person of ordinary skill in the art attempting to obtain a claimed antibody that is not disclosed or a variant of a disclosed antibody "would have to do essentially the same amount of work as the inventors of the patents-in-suit." *MorphoSys AG*, 358 F. Supp. 3d at 372.

Even taking the testimony in the light most favorable to Plaintiffs, the testimony of Plaintiffs' own experts indicates that the experimentation necessary to enable the full scope of the claims would take a substantial amount of time and effort. Dr. Rees' own testimony indicated that despite routine techniques and low cost, it would be impractical for a person of ordinary skill in the art to generate large pools of antibodies (as the patent's "roadmap"

requires) and that the "roadmap" requires "essentially the same amount of work as the inventors of the patents-in-suit" did to discover the invention. *MorphoSys AG*, 358 F. Supp. 3d at 372. Thus, a reasonable factfinder could only have determined that the experimentation necessary to enable the full scope of the claims would take a substantial amount of time and effort.

f. Summary of the *Wands* Factors

In light of the factual conclusions above, any reasonable factfinder would find that practicing the claims' full scope would require substantial experimentation. The remaining question is whether a reasonable factfinder could not fail to find that the experimentation required is "undue." Defendants assert that *MorphoSys AG* v. *Janssen Biotech*, *Inc.*, 358 F. Supp. 3d 354 (D. Del. 2019), should control my determination. Plaintiffs attempt to distinguish *MorphoSys* on the basis that the patentee in that case "did not establish that the claimed genus was small or that routine techniques could be employed to practice the full scope of the genus." (D.I. 923 at 17).

I agree with Defendants that *MorphoSys* is instructive. First, as I determined above, there does not appear to be a genuine dispute that the number of antibodies potentially falling within the claim scope is in the millions. Second, there does not appear to be a genuine dispute that substitution of amino acids in a sequence may have unpredictable effects on the function of the antibody. Third, the techniques employed to identify antibodies within the full scope of the genus are routine. Fourth, despite the routine techniques employed, it appears that a person of ordinary skill in the art would still be required "to do essentially the same amount of work as the inventors of the patents-in-suit," *MorphoSys AG.*, 358 F. Supp. 3d at 372, or engage in a trial-and-error process of amino acid substitution as

even conservative substitutions may have unexpected results. Fifth, the specifications do not provide guidance on how to predict the effect of the sequence on the function of the antibody. The "roadmap" disclosed by the patents is almost exactly the same as the patentee's initial research process to discover the twenty-six disclosed antibodies. Finally, a reasonable factfinder could only conclude that the amount of time and effort required to enable the full scope of the claims would be substantial. Therefore, I determine as a matter of law that undue experimentation would be needed to practice the full scope of the claimed invention.

Further comparison with precedent from the Federal Circuit and this Court supports these conclusions. As in *Wyeth*, there is "no genuine dispute that it would necessary to first synthesize and then screen each candidate [antibody] using the assays disclosed in the specification to determine whether it has" binding and blocking effects. 720 F.3d at 1385. Additionally, the art in *Wyeth* and the art here are unpredictable, and the specification "discloses only a starting point for further iterative research." *Id.* at 1386. As in *Idenix Pharms.*, where there was a broader class of compounds that required testing to determine if they met functional limitations, it is "only through experimentation, not prediction" that a person of ordinary skill in the art could conclude that a particular antibody would meet the binding and blocking requirements of the claim. 2018 WL 922125 at *23.[11]

Thus, the claims are not enabled, and I will grant Defendants' motion for judgment as a matter of law for lack of enablement.

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[11] The Federal Circuit heard argument on the appeal from this decision on July 9, 2019.

C. NEW TRIAL

"If the court grants a renewed motion for judgment as a matter of law, it must also conditionally rule on any motion for a new trial by determining whether a new trial should be granted if the judgment is later vacated or reversed." Fed. R. Civ. P. 50(c)(1). Thus, I will now address Defendants' motion for a new trial.

1. Clear Weight of the Evidence

For the reasons stated above addressing the 50(b) motion, I do not find the jury verdict on written description to be against the clear weight of the evidence or require a new trial to prevent a miscarriage of justice.

On the issue of enablement, I must conditionally decide the motion for a new trial with the assumption that the appellate court reversed or vacated the grant of the renewed JMOL motion. It was Defendants' burden at trial to show that the asserted claims were not enabled by clear and convincing evidence. I determine that if the JMOL of no enablement is reversed, the jury verdict that the asserted claims were enabled was not against the clear weight of the evidence and a new trial need not be granted to prevent a miscarriage of justice.

2. Post-Priority Date Evidence

Defendants argue that a new trial should be granted because I erroneously excluded post-priority-date evidence. (D.I. 885 at 2). I disagree. The thrust of Defendants' argument seems to be that I disregarded the Federal Circuit's mandate from the first appeal in this suit and that the Federal Circuit therein said that post-priority-evidence is always relevant to demonstrating a lack of written description or enablement. (*Id.* at 2-3). Defendants misread the Federal Circuit's opinion.

The Federal Circuit held that "[i]t was [ ] legal error for the district court to *categorically* preclude all of [Defendants'] post-priority-date evidence of Praluent and other antibodies." *Amgen Inc.* v. *Sanofi*, 872 F.3d 1367, 1375 (Fed. Cir. 2017). More specifically, for written description purposes, the Federal Circuit distinguished between the prohibition on "post-priority-date evidence proffered to illuminate the post-priority-date state of the art, which is improper, [and] post-priority-date evidence proffered to show that a patent fails to disclose a representative number of species," which it held to be proper. *Id.* at 1374-75. For purposes of enablement, the Federal Circuit stated that post-priority-date evidence showing lengthy and potentially undue experimentation to enable the full scope of the claims "could have been relevant to determining if the claims were enabled as of the priority date and should not have been excluded simply because it post-dated the claims' priority date." *Id.* at 1375 (emphasis added). However, the Federal Circuit did not state that post-priority-date evidence would always be admissible for these purposes.

In my second order on motions in limine, I excluded post-priority-date evidence related to Plaintiffs' research program for catabolic antibodies presented to show a lack of enablement under FRE 402 and 403. I determined that the evidence was irrelevant to the issue of enablement because the research program reflected a subsequent state of the art and therefore should be excluded under FRE 402. I also determined that to the extent there was any probative value, the evidence, if offered to prove enablement was likely to confuse the issues, mislead the jury, and waste time, such that the evidence's probative value was substantially outweighed by those concerns and should be excluded under FRE 403. (D.I. 693 at 3).

At trial, after further argument by the parties, I determined that certain documents could have been relevant to enablement, but only if Defendants could "first establish that [Dr. Jackson] was trying to make other antibodies within the scope of the patent." (D.I. 864 at 570). Defendants did not make this showing, and thus, I continued to exclude these documents for the reasons stated in the order on motions in limine.

Regarding enablement, Defendants argue that the excluded evidence would have shown that "Amgen continued to look for [antibodies similar to the Competitor Antibodies] for more than four years after the priority date and never found them." (D.I. 885 at 5). However, the documents they cite did not actually show that. Defendants submitted no evidence into the record that Amgen was continuing to look for antibodies from 2008 to 2012. The only cited documents are from March 2012 to June 2012, a relatively short period of time. They do not show that the patentee "engaged in lengthy and potentially undue experimentation" over the four-year period to enable the claim scope. *Amgen*, 872 F.3d at 1375. Thus, the documents are irrelevant to the issue of enablement. To the extent the documents have any marginal relevance, the probative value was substantially outweighed by the likelihood of jury confusion because the documents arose in a subsequent state of the art and a subsequent research program into "catabolic" antibodies. (D.I. 763 at 3).

Regarding written description, I did not exclude documents when ruling on the motion in limine. (*Id.* at 2-3). However, when presented with specific documents and questions at trial, I did exclude a subset of documents that Defendants sought to introduce at trial. At trial, Defendants' attorneys asked, "Were there any documents from Amgen that you considered which confirm your opinion

that you just gave that Amgen's claims fail to satisfy the written description requirement?" (D.I. 863 at 211:9-12). Plaintiffs objected, arguing that the question was designed to elicit irrelevant documents and conflate "actual" possession of a species with possession of a representative species. (*Id.* at 211:15-212:6, 212:18-23). Defendants responded that the documents they sought to admit demonstrated that "Amgen was aware . . . that EGFa mimics were a separate category of antibodies which they failed to have." (*Id.* at 213:1-5). Plaintiffs responded that the documents were related to a subsequent state of the art and did not serve the purpose of determining whether a person of ordinary skill in the art in 2008 would have found any disclosed antibody to be representative of the Competitor Antibodies. (*Id.* at 213:6-11). I sustained Plaintiffs' objection because the written description inquiry is an objective inquiry and the experts could testify as to whether the disclosed antibodies were representative (or not) of the competitor antibodies. (*Id.* at 215:8-16).

The second instance related to written description at trial occurred as follows. Defendants asked Dr. Jackson if his team "monitored specifically Regeneron PCKS9 research?" (D.I. 864 at 542:11-13). Plaintiffs objected to the question as violating the MIL order. (*Id.* at 542:13). At sidebar, Defendants asserted the question should be allowed because of follow-up questioning as to whether Dr. Jackson found Praluent in the pre-patent work, reading from a specific document. (*Id.* at 542:20-543:6). I sustained the objection under the MIL because "whether or not they developed Praluent as part of the patent is actually irrelevant" to the issue of written description because a patentee does not have to describe every species in a genus to have adequately described the claims. (*Id.* at 543:22-24).

After the conclusion of testimony that day, I heard further argument from the parties on the documents Defendants sought to introduce with Dr. Jackson. I determined that for the purposes of Dr. Jackson's testimony, the documents would be excluded for the purposes of written description as "irrelevant to the written description issues" and that "to the extent there is any marginal relevance, [] the confusion would substantially outweigh the probative value." (*Id.* at 569:15-21).

Defendants argue that the excluded documents would have shown that (1) "Amgen monitored Regeneron/Sanofi, Pfizer, and Merck . . . and made the Competitor Antibodies based on published sequence information," (D.I. 885 at 6)[12], (2) Amgen "found the Amgen Antibodies different from the Competitor Antibodies in ways that were directly relevant to the claims, including where they bind to PCSK9," (*id.*)[13] (3) Amgen had a "missing epitope" (*id.* at 7), and (4) Amgen did not have an EGFa mimic (*id.*).

First, whether Plaintiffs monitored their competitors and made the Competitor Antibodies based on published sequence information is irrelevant to the objective inquiry of written description. It is irrelevant to written description that Plaintiffs did not make the Competitor Antibodies until the sequence information was published; written description does not require actual reduction to practice. Rather, the specification must demonstrate possession. Whether an inventor actually made a specific embodiment before filing the patent is irrelevant.

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[12] Defendants point to the following excluded documents for these points: Exs. 4-14 (DTX3137, DTX3147, DTX3155, DTX3156, DTX3170, DTX3171, DTX3188, DTX3141, DTX3173, DTX3190, and DTX3198).

[13] Ex. 5 (DTX3147, Ex. 15 (DTX3191), Ex. 16 (DTX3205).

Second, the documents Defendants cite for their second assertion are also irrelevant to the issue of written description. Exhibit 16 (DTX 3205) does not make any comparison between the Amgen antibodies and the competitor antibodies. Exhibit 5 states, "316P is a different PCKS9 antibody. We also did not get this one from PCSK9#l" in the context of a previous comparison of another Regeneron antibody to two Amgen antibodies (8A3 and 11F1). This statement is also irrelevant to the issue of written description because being a "different antibody" does not equate to being a non-representative antibody. Exhibit 15 is also irrelevant to the issue of written description because it does not compare the Rinat antibody to the antibodies disclosed in the patent. To the extent this document had any marginal relevance, its probative value was substantially outweighed by the likelihood of jury confusion due to these documents arising in research project at a subsequent state of the art.

Third, as to both the "missing epitope" and the "EGF-a mimic" that Defendants allege the excluded documents would show, the evidence is irrelevant to written description. As I stated at trial, merely saying the patentee didn't have "X" is irrelevant for written description because "actual possession" is not required. Furthermore, written description is an objective inquiry into what a person of ordinary skill in the art would have understood at the time the patent application was filed. Defendants never established that a person of ordinary skill in the art in 2008 would have known or considered the EGF-a binding region or the missing epitope in determining whether the disclosed patents were representative of the Competitor Antibodies. Finally, even if there was error in excluding these documents, there was no prejudice to the Defendants. Defendants submitted significant expert testimony

to the jury that the disclosed antibodies were not representative of the Competitor Antibodies because of the difference in the binding region and the "missing epitope."

Thus, I determine that the documents were properly excluded under FRE 402 and 403, and a new trial is thus unwarranted.

3. Representative Species Jury Instruction

Defendants assert that "a new trial should be granted because the Court failed to instruct the jury that the patent must describe antibodies representative of the infringing product." (D.I. 885 at 13). Defendants requested that I include the following statement in the jury instruction for written description:

> When a patent owner asserts that an antibody made by other companies like Defendants falls within the scope of its claimed genus of antibodies, the patent must at least describe some antibody or antibodies representative of antibodies that are structurally similar to the Defendants' antibody (and other third-party antibodies that fall within the scope of the claim) in order to meet the written description requirement.

(D.I. 791-1 at 12-13). Defendants also requested this jury instruction at the first trial. It was not given in the first trial. Defendants did not appeal the Court's decision not to give this instruction. Upon remand and reassignment of this case to me, I stated that the parties could "propose changes to the . . . final jury instructions . . . from the first trial that reflect new developments in the law or the record at trial, and the reassignment of the case to [me]." (D.I. 458 at 12).

First, I note that Defendants' proposed inclusion of this language was not motivated by a new development in the

law or the record at trial. The case Defendants rely on, *AbbVie*, was decided in 2014, well before the first trial. *AbbVie*, 759 F.3d 1285 (Fed. Cir. 2014) (decided on July 1, 2014; (D.I. 1 (filed Oct. 17, 2014)).

Second, I note that Defendants did not appeal the Court's decision not to include this language in the jury instructions. "An issue that falls within the scope of the judgment appealed from but is not raised by the appellant in its opening brief on appeal is necessarily waived." *Engel Indus., Inc.* v. *Lockformer Co.*, 166 F.3d 1379, 1383 (Fed. Cir. 1999). I determine that the jury instruction issue was thus waived by Defendants.

Third, even if the jury instruction issue were not waived, it was not error to not include this language. As I recognized, this language, while coming from *AbbVie*, was repetitive of the underlying principle stated in a more neutral fashion earlier on in the paragraph: "When there is a substantial variation within the claimed genus, the specifications must describe a sufficient variety of species to reflect the variation within the claimed genus." (D.I. 865 at 831:9-11; D.I. 812 at 14).

Thus, declining to include Defendants' specific language in the representative species jury instruction does not warrant the grant of a new trial.

4. Alleged Inherent Data / Improper Inherency Jury Instruction

Defendants argue that the admission of post-priority-date data was improper because the data was not included in the patents.

I disagree with Defendants. Data admission was proper to illuminate the state of the art at the priority date, show enablement, and to demonstrate inherent properties of antibodies that may be relevant to the

representative species test. The Federal Circuit has held, "There is no requirement that an invention's properties and advantages were fully known before the patent application was filed . . . [n]or is it improper to conduct additional experiments and provide later-obtained data in support of patent validity." *Knoll Pharm Co.* v. *Teva Pharms. USA*, 367 F.3d 1381, 1385 (Fed. Cir. 2004). It is not contested that a person of ordinary skill in the art could have used the routine techniques of x-ray crystallography and alanine scanning at the time the patent application was filed to determine the binding properties of these antibodies.

Defendants also challenge the inclusion of a jury instruction regarding inherency. The jury instruction reads,

> Under the doctrine of inherent disclosure, when a specification describes an invention that has certain undisclosed yet inherent properties, those inherent properties may be relied upon for written description support. To be inherent, the feature that is alleged to have been inherent must necessarily have existed in the specification. The fact that the feature is likely to have existed is not sufficient. It is not required, however, that persons of ordinary skill recognize or appreciate the inherent disclosure at the time the January 9, 2008 application was filed.

(D.I. 812 at 13-14). Defendants cite *Tronzo* v. *Biomet, Inc.*, 156 F.3d 1154, 1159 (Fed. Cir. 1998), for the proposition that the instruction was improper "because the allegedly 'inherent disclosure' was not 'necessarily . . . present' in all example provided in the specification." (D.I. 885 at 20). But *Tronzo* requires solely that "the missing descriptive matter must necessarily be present in the . . . specification such that one skilled in the art would recognize such

a disclosure." 156 F.3d at 1159. Here, the structural data is necessarily present in the specification for antibodies that are disclosed by sequence; a person of ordinary skill in the art could make the antibodies and use routine techniques to discover the data that Plaintiffs relied upon here. See *Ariad*, 598 F .3d at 1351 (enumerating a number of factors for evaluating adequacy of disclosure including existing knowledge in particular field). The facts here are analogous to those in *Kennecott Corp.* v. *Kyocera Intern., Inc.*, 835 F.2d 1419, 1423 (Fed. Cir. 1987), where "anyone with a microscope would see the microstructure of the product." Defendants attacks the applicability of *Kennecott* because in that case, every example produced a ceramic that had an equiaxed structure, whereas here, there were some examples that fell outside the claims. (D.I. 885 at 15-16). But *Kennecott* did not involve genus claims. 835 F.2d at 1420. Where the inquiry is whether the disclosed species are representative, the inherent disclosure need not be common to every species. Thus, *Kennecott* applies here. The instruction was not error.

IV. CONCLUSION

For the foregoing reasons, Defendants' Motion for Judgment as a Matter of Law is granted-in-part and denied-in-part. Defendants' Motion for a New Trial is conditionally denied. Plaintiffs' Motion for Permanent Injunction will be dismissed as moot. An accompanying order will be entered.

APPENDIX C

IN THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

CIVIL ACTION NO. 14-1317-RGA

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AND AMGEN USA, INC.,

Plaintiffs,

v.

SANOFI, SANOFI-AVENTIS U.S. LLC, AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC., AND REGENERON PHARMACEUTICALS, INC.,

Defendants.

ORDER

For the reasons stated in the accompanying opinion, IT IS HEREBY ORDERED that Defendants' Motion for Judgment as a Matter of Law (D.I. 886) is GRANTED for lack of enablement and DENIED as to written description. Defendants' Motion for a New Trial (D.I. 883) is conditionally DENIED. Plaintiffs' Motion for Permanent Injunction (D.I. 871) is DISMISSED as moot.

Entered this 28 day of August, 2019.

/s/ Richard G. Andrews
United States District Judge

APPENDIX D

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

C.A. NO.: 14-1317-RGA
(CONSOLIDATED)

JURY TRIAL DEMANDED

AMGEN INC.; AMGEN MANUFACTURING, LIMITED; AND AMGEN USA INC.,

Plaintiffs,

v.

SANOFI; SANOFI-AVENTIS U.S. LLC; AVENTISUB LLC, f/d/b/a AVENTIS PHARMACEUTICALS INC.; AND REGENERON PHARMACEUTICALS, INC.,

Defendants.

~~[PROPOSED]~~ FINAL JUDGMENT

Pursuant to the Court's memorandum opinion (D.I. 1050) and order (D.I. 1051) entered on August 28, 2019, and all prior ~~[**BY AMGEN:** related or underlying]~~ rulings, orders, judgments and findings, IT IS ORDERED AND ADJUDGED that Judgment be and is hereby entered in favor of Defendants Sanofi, Sanofi-Aventis, U.S. LLC, Aventisub, LLC, and Regeneron Pharmaceuticals, Inc. and against Plaintiffs Amgen Inc., Amgen Manufacturing Limited, and Amgen USA, Inc.

SO ORDERED this 3 day of October, 2019.

/s/ Richard G. Andrews
United States District Judge

APPENDIX E

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

2020-1074

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,

Plaintiffs-Appellants,

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,

Defendants-Appellants.

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews

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JEFFREY A. LAMKEN, MoloLamken LLP, Washington, DC, filed a petition for rehearing en banc for plaintiffs-appellants. Also represented by SARAH JUSTINE NEWMAN, MICHAEL GREGORY PATTILLO, JR.; SARA MARGOLIS, New York, NY; EMILY JOHNSON, ERICA S. OLSON, STEVEN TANG, STUART WATT, WENDY A. WHITEFORD, Amgen Inc., Thousand Oaks, CA; KEITH HUMMEL, Cravath Swaine & Moore LLP, New York, NY; WILLIAM G. GAEDE, III, McDermott Will & Emery LLP, Menlo

Park, CA; CHRISTOPHER B. MEAD, Schertler Onorato Mead & Sears LLP, Washington, DC; JAMES L. HIGGINS, MELANIE K. SHARP, Young, Conaway, Stargatt & Taylor, LLP, Wilmington, DE. Plaintiff-appellant Amgen Inc. also represented by SARAH CHAPIN COLUMBIA, McDermott, Will & Emery LLP, Boston, MA; LAUREN MARTIN, Quinn Emanuel Urquhart & Sullivan LLP, Boston, MA.

MATTHEW WOLF, Arnold & Porter Kaye Scholer LLP, Washington, DC, filed a response for defendants-appellees. Also represented by VICTORIA REINES; DAVID K. BARR, DANIEL REISNER, New York, NY; DEBORAH E. FISHMAN, Palo Alto, CA; GEORGE W. HICKS, JR., NATHAN S. MAMMEN, CALVIN ALEXANDER SHANK, Kirkland & Ellis LLP, Washington, DC. Defendants-appellees Sanofi, Aventisub LLC, Sanofi-Aventis U.S. LLC also represented by STEPHANIE DONAHUE, Sanofi, Bridgewater, NJ. Defendant-appellee Regeneron Pharmaceuticals Inc. also represented by LARRY A. COURY, LYNDA NGUYEN, Regeneron Pharmaceuticals Inc., Tarrytown, NY.

MARK A. LEMLEY, Stanford Law School, Stanford, CA, for amici curiae Ann Bartow, Timothy Richard Holbrook, Mark David Janis, Dmitry Karshtedt, Mark A. Lemley, Stephen McJohn, Robert P. Merges, Sean B. Seymore.

JEFFREY PAUL KUSHAN, Sidley Austin LLP, Washington, DC, for amici curiae Biogen Inc., Bristol-Myers Squibb Company, Corning Incorporated, Merck Sharp & Dohme Corp. Also represented by STEVEN J. HOROWITZ, Chicago, IL; SUE WANG, San Francisco, CA.

JOHN M. DESMARAIS, Desmarais LLP, New York, NY, for amicus curiae GlaxoSmithKline PLC. Also represented by ELIYAHU BALSAM, TODD LAWRENCE KRAUSE.

ON PETITION FOR REHEARING EN BANC

Before MOORE, *Chief Judge*[*], NEWMAN, LOURIE, DYK, PROST[**], O'MALLEY, REYNA, TARANTO, CHEN, HUGHES, and STOLL, *Circuit Judges*.[***]

LOURIE, *Circuit Judge*, with whom PROST and HUGHES, *Circuit Judges*, join, authored a separate opinion on the denial of the petition for panel rehearing.

PER CURIAM.

ORDER

Amgen Inc., Amgen Manufacturing, Limited, and Amgen USA, Inc. filed a petition for rehearing en banc. A response to the petition was invited by the court and filed by Sanofi, Aventisub LLC, Sanofi-Aventis U.S. LLC, and Regeneron Pharmaceuticals Inc. A group of intellectual property professors; GlaxoSmithKline plc; and Biogen Inc., Bristol-Myers Squibb Company, Corning Incorporated, and Merck Sharp & Dohme Corp. requested leave to file briefs as amici curiae, which the court granted. The petition was first referred as a petition for rehearing to the panel that heard the appeal, and thereafter the petition for rehearing en banc was referred to the circuit judges who are in regular active service.

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[*] Chief Judge Kimberly A. Moore assumed the position of Chief Judge on May 22, 2021.

[**] Circuit Judge Sharon Prost vacated the position of Chief Judge on May 21, 2021.

[***] Circuit Judge Evan J. Wallach assumed senior status on May 31, 2021, and did not participate in the decision on the petition for rehearing en banc.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is denied.

The petition for rehearing en banc is denied.

The mandate of the court will issue on June 28, 2021.

FOR THE COURT

June 21, 2021
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

**UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT**

2020-1074

AMGEN INC., AMGEN MANUFACTURING, LIMITED, AMGEN USA, INC.,

Plaintiffs-Appellants,

v.

SANOFI, AVENTISUB LLC, FKA AVENTIS PHARMACEUTICALS INC., REGENERON PHARMACEUTICALS INC., SANOFI-AVENTIS U.S. LLC,

Defendants-Appellants.

Appeal from the United States District Court for the District of Delaware in Nos. 1:14-cv-01317-RGA, 1:14-cv-01349-RGA, 1:14-cv-01393-RGA, 1:14-cv-01414-RGA, Judge Richard G. Andrews

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LOURIE, *Circuit Judge*, with whom PROST and HUGHES, *Circuit Judges*, join, authoring a separate opinion on the denial of the petition for panel rehearing.

Amgen has petitioned for panel rehearing. The petition is denied.

Amgen argues that we have created a new test for enablement. That is incorrect. It has always been, or at least has been since the Patent Act of 1870, that a patent applicant must enable one's invention, whatever the invention is. See Section 26, Patent Act of 1870, 16 Stat.

198 (1870), (R.S. § 4888). A composition of matter, whether a chemical compound or biological material, accordingly, must be enabled, as must other types of inventions.

If the invention is a group of compositions, defined as a genus, that group is enabled by a disclosure commensurate with the scope of the genus. For years, before biological materials were often claimed, chemical genus claims were enabled by actual or constructive (often called prophetic) examples. Chemical patent specifications were filled with examples of compounds that had been prepared, generally shown by use of the past tense to describe the procedures, with melting points or other physical constants obtained by actual reductions to practice. Constructive examples were described in the present tense, with starting materials and process details resulting in named compounds within the scope of the claims. Whether actual or constructive, those examples enabled the full scope of the claims. Such well-supported generic claims do not lack for enablement, or written description. Amici and others bemoaning the so-called death of generic claims are therefore off-base. Genus claims, to any type of invention, when properly supported, are alive and well.

What is new today is not the law, but generic claims to biological materials that are not fully enabled. Enablement is required, even for generic claims to biological materials. But, as with genus claims to chemical compounds, if they encompass more subject matter than just a few species, they need to be enabled accordingly. Biological compositions not actually prepared need to be described constructively, if required to enable the full scope of the claims, with procedures and names of resultant compositions, as with chemical compositions.

Amgen and amici argue that requiring that broad generic claims in the biotechnology field be supported by disclosure enabling the full scope of the claims will make it impossible to obtain proper protection for biotechnology inventions. But all that the enablement requirement precludes is obtaining protection for inventions broader than are disclosed or enabled, and that were apparently not invented by the applicant or patentee, as shown by a lack of enabling disclosure. If the genus had been invented by the time of filing, it would have been fully enabled in the patent.

Entitlement to broad genus claims thus requires disclosure and enablement of species supportive of the genus that a patentee claims to have invented. That requirement is based on the concept that in order to have invented a genus, one needs to have invented species that constitute the genus. Drawing a broad fence around subject matter, without filling in the holes, is not inventing the genus. It in fact discourages invention by others. If one has disclosed or enabled only a small number of invented species, then one has not invented a broad genus. Invention of a genus means to conceive and reduce to practice a reasonable number and distribution of species constituting the genus. Mere statement of a genus does not demonstrate that one has invented a generic concept, without the enablement of constituent species.

Amici insist that this court has recently adopted a "numbers-based standard" to evaluate enablement, asking not whether experimentation is undue but how long it would take to make and screen every species. IP Professors' Amicus Br. 7. That mischaracterizes our law, and our opinion specifically resisted what might be termed a simple "numerosity" or "exhaustion" requirement. Consistent with our law, the opinion examined the relevant

Wands factors and their interaction in a case-specific manner. The problem was not simply that the claimed genus was numerous—it was that it was so broad, extending far beyond the examples and guidance provided. Likewise, it was not that it would take a long time to collect the full set of each and every embodiment—it was that the narrow and limited guidance in the specification made far corners of the claimed landscape that were particularly inaccessible or uncertain to make unenabled.

Amgen and its amici argue that our decisions on enablement (just as it was once argued with respect to written description) threaten innovation and will "devastate" the incentives to invest in drug discovery. It seems to them that the sky is falling. But enablement is part of our law, and for good reason. One should not gain exclusivity over claimed subject matter without disclosing how to make and use it. And if one considers that one has invented a group of compositions defined by a genus but does not know enough to fully enable that genus, one would suppress innovation if one were able to claim such a broad genus, not enhance it. Amgen, by asserting such broad, unsupported claims is doing just that, by trying to control what it has not invented. And, contrary to assertions by amici that broad, unenabled claims are necessary to protect investment, claims to materials properly supported by inventive work and disclosure can be protected. Amgen in fact has separate patent protection on the PCSK9 antibody that it has invented and additionally purports to cover by the generic claim we have invalidated. See U.S. Patent 8,030,457. Thus, the failure to obtain unsupported, unenabled claims has not deprived it of patent protection on the fruits of its investment.

Additionally, if another party invents a species not described or enabled by a first inventor, and hence not able

to be encompassed by a properly enabled generic claim, that party has promoted the progress of the useful arts. Yet if that compound is so close to species disclosed and claimed by a first entrant as to be an equivalent, there is the doctrine of equivalents to protect the innovator. And, of course, that second comer may encounter the expensive hurdle of having to meet its own regulatory requirements, if it does not qualify for ANDA or biosimilar status.

Claims defining a composition of matter by function raise special problems because one may not know whether a species is within the scope of a generic claim until one has made it and one can ascertain whether it possesses the claimed function, hence that it has been enabled. In such cases, it is circular; enablement comes only with success, which depends upon enablement. It is not the law that one can put forth an idea, or a result or function, and claim all methods of achieving it; one cannot claim everything that works.

This court has already considered the impact of functional means claim limitations on whether a disclosure is commensurate in scope with the claim. The answer is that single means claims claim too much. See *In re Hyatt*, 708 F.2d 712, 714 (Fed. Cir. 1983) (Rich, J.) ("The proper statutory basis for the rejection of a single means claim is the requirement of the first paragraph of § 112 that the enabling disclosure of the specification be commensurate in scope with the claim under consideration. The long-recognized problem with a single means claim is that it covers every conceivable means for achieving the stated result, while the specification discloses at most only those means known to the inventor."). Multiple means claims simply compound the problem.

Amgen argues that we should overrule case law that holds that enablement is a question of law, albeit based

on underlying factual findings. But we are bound by our precedent and decline to recommend to the court that it go en banc to overrule longtime precedent simply because a party has questioned it. One can reasonably ask, as Amgen does, why enablement is a question of law when written description, which sits side by side with the enablement requirement, is not. They both relate to the disclosure in the patent specification. But our precedent is long in the tooth, dating back before the establishment of this court. See *Raytheon Co.* v. *Roper Corp.*, 724 F.2d 951, 960 n.6 (Fed. Cir. 1983), cert. denied, 469 U.S. 835 (1984) (citing *In re Hogan*, 559 F.2d 595, 604 (C.C.P.A. 1977) (stating that "Courts should not treat the same *legal* question, enablement under § 112, in one manner with respect to the applicant and in a different manner with respect to the examiner.") (emphasis added); *In re Brandstadter*, 484 F.2d 1395, 1406 (C.C.P.A. 1973) (analyzing whether certain affidavits could be considered when evaluating "the ultimate *legal question* of enablement.") (emphasis added)); see also *Amgen, Inc.* v. *Chugai Pharm. Co.*, 927 F.2d 1200, 1216 (Fed. Cir. 1991), cert. denied, 502 U.S. 856 (1991) (citing *Moleculon Research Corp.* v. *CBS, Inc.*, 793 F.2d 1261, 1268 (Fed. Cir. 1986), cert. denied, 479 U.S. 1030 (1987)) ("We review a determination of enablement as a *question of law*.") (emphasis added); *Elan Pharms., Inc.* v. *Mayo Found. for Med. Educ. & Research*, 346 F.3d 1051, 1054 (Fed. Cir. 2003) (citing *Enzo Biochem, Inc.* v. *Calgene, Inc.*, 188 F.3d 1362, 1369 (Fed. Cir. 1999)) ("[W]hether a disclosure is enabling . . . is a *question of law* . . . .") (emphasis added); *McRO, Inc.* v. *Bandai Namco Games Am., Inc.*, 959 F.3d 1091, 1096 (Fed. Cir. 2020) (citing *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013)) ("[W]hether a patent satisfies the enablement requirement is a *question of law* . . . .") (emphasis added).

The much-cited *Wands* case is the signature authority on the issue. See *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988) (explaining that "we review enablement as a *question of law*.") (emphasis added).

Indeed, despite being repeatedly asked over the decades this court has existed, the Supreme Court has not seen fit to take up this question. It has, however, made clear that interpretation of claim scope, a question inexorably intertwined with enablement, is a question of law. Obviousness, which involves comparing claim scope with the prior art, is similarly a question of law. And so it is no surprise that enablement, which involves interpreting the specification and the scope of the claims, is also a question of law, if one that accommodates underlying factual inquiries where applicable. Thus, the principle is indelibly embodied in and consistent with our law, and we see no reason to change it, especially where the arguments that Amgen makes provide no compelling reason to introduce such a seismic shift.

Accordingly, the petition for panel rehearing is denied.

APPENDIX F
RELEVANT STATUTORY PROVISION

The Patent Act, 35 U.S.C. § 1 *et seq.*, provides in relevant part:

§ 112. Specification

(a) IN GENERAL.—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, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

* * * * *