2020-1074

United States Court of Appeals for the Federal Circuit

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

Plaintiffs-Appellants

v.

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

Defendants-Appellees

Appeal from the United States District Court for the District of Delaware in No. 14-01317-RGA

BRIEF OF AMICI CURIAE BRISTOL-MYERS SQUIBB COMPANY AND MERCK SHARP & DOHME CORP. IN SUPPORT OF AMGEN INC.

Jorge A. Goldstein
Eldora L. Ellison
Kristina Caggiano Kelly
William H. Milliken
Sterne Kessler Goldstein & Fox PLLC
1100 New York Ave., N.W.
Washington, DC 20005
202.371.2600

Counsel for Amici Curiae Bristol-Myers Squibb Company and Merck Sharp & Dohme Corp.

FORM 9. Certificate of Interest **Form 9**
Rev. 10/17

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

Amgen Inc. **v.** Sanofi

Case No. 20-1074

CERTIFICATE OF INTEREST

Counsel for the:
☐ (petitioner) ☐ (appellant) ☐ (respondent) ☐ (appellee) ■ (amicus) ☐ (name of party)

Bristol-Myers Squibb Company and Merck Sharp & Dohme Corp.

certifies the following (use "None" if applicable; use extra sheets if necessary):

1. Full Name of Party Represented by me	2. Name of Real Party in interest (Please only include any real party in interest NOT identified in Question 3) represented by me is:	3. Parent corporations and publicly held companies that own 10% or more of stock in the party
Bristol Myers Squibb Company	N/A	None
Merck Sharp & Dohme. Corp.	N/A	Merck & Co., Inc

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5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. *See* Fed. Cir. R. 47. 4(a)(5) and 47.5(b). (The parties should attach continuation pages as necessary).

None.

2/28/2020
Date

/s/ Jorge A. Goldstein
Signature of counsel

Please Note: All questions must be answered

Jorge A. Goldstein
Printed name of counsel

cc: Counsel of Record

Reset Fields

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AMICI CURIAE'S STATEMENT UNDER RULE 29

Pursuant to Federal Rule of Appellate Procedure Rule 29(c)(5)(A)-(C), amici curiae confirm that no party's counsel involved in the litigation below authored this brief, in whole or in part. Counsel for amici confirm that, while they are counsel for Party Amgen on other matters, they are not counsel in the present matter. Amici also confirm that no party or party's counsel, or any other person other than the amici, contributed money that was intended to fund preparing or submitting this brief.

INTEREST OF AMICI CURIAE

Amicus Bristol-Myers Squibb Company is an innovator biotechnology company that researches targeted treatments for human disease. Amicus Merck Sharp & Dohme Corp. is an American multinational pharmaceutical company and one of the largest pharmaceutical innovators in the world.

Amici rely on the patent system to protect their groundbreaking inventions and discoveries related to such medicines and associated methods of treatment. Amici believe that the decision below undermines patent protection for innovative medical treatments and the molecules involved. If that decision is allowed to stand, amici and other innovator biotechnology companies may be unable to obtain sufficient patent protection on their discoveries. That, in turn, could slow the pace of research and development and hinder innovation to the detriment of patients and physicians. If the law continues to evolve such that patent protection requires prohibitive and unnecessary disclosure, companies may no longer see innovation as a viable pursuit.

INTRODUCTION

Many modern therapies are based on understanding and modulating the biological targets that give rise to disease—for example, identifying and manipulating molecular receptors that signal a cell's growth or death. Monoclonal antibodies—the category of therapeutics at issue in this appeal—can block or

activate such targets with great specificity and thereby provide effective medical treatment with minimal side effects. Antibody-based therapies have revolutionized modern medicine and led to unprecedented success in treating various cancers, autoimmune diseases, and other conditions, many of which previously had no known treatment.

In 2018 (the most recent year for which data are available), therapeutic antibodies represented five out of the top ten most-prescribed pharmaceutical products: Avastin® (cancer), Remicade® (rheumatoid arthritis), Herceptin® (cancer), Rituxan® (autoimmune diseases and cancer), and Humira® (autoimmune diseases). Other antibody-based drugs, like Yervoy®, Opdivo®, and Keytruda®, have revolutionized immuno-oncology, creating an entirely new approach to treating and potentially curing a variety of cancers. As researchers continue to unlock the enormous potential of antibody-based treatments, the outsized impact of antibody drugs on the medical landscape is only likely to grow.

The first step in developing an antibody-based therapy is to discover in the body the underlying molecular target to which the antibody binds, the connection between the target and the disease, and the pathways that the antibody may activate or inhibit. Next, the inventor must assess whether an antibody can be generated that will effectively modulate the target, and if so, find a way to produce that antibody on a sufficiently large scale to manufacture and commercialize it, and test

the resulting antibody for safety and efficacy, eventually in large-scale clinical trials.

This process is complex and expensive. The cost of bringing a biologic (the category of drugs of which antibodies are a part) to market averages $2.6 billion. In the last decade, biopharmaceutical companies like the amici here have invested hundreds of billions of dollars in research and development. In 2016 alone, biopharmaceutical companies invested about $90 billion in R&D in the United States. On average, the biopharmaceutical industry invests six times more in R&D as a percentage of sales than any other manufacturing industry in this country. To ensure that these innovator companies receive a reasonable return on their investments—and thus that they are incentivized to make the investments in the first place—it is critical that the companies be able to obtain reliable and robust patent protection on their inventions.

But obtaining robust patent protection is easier said than done. Given the lack of eligibility of natural materials and phenomena, *see, e.g.*, *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013); *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66 (2012), patent protection may not be available for the underlying molecular targets and pathways. Instead, the innovator must obtain patents on the molecules (antibodies in this case) that interact with the targets and modulate the pathways. It is therefore

crucial that innovators in this space be able to obtain broad patent protection on the antibodies themselves or on methods of using them.

Once the innovator has discovered the underlying target and connection to disease, and raised an antibody capable of effectively binding to that target, however, it may be routine and conventional to manufacture similar antibodies that also effectively bind to that target and treat the same disease. These follow-on antibodies that fall within the genus may differ from the first-discovered antibody in certain ways (for example, in the specific sequence of amino acids) but such differences are not medically significant. As technology has improved, the speed and effectiveness of testing such antibodies for the required binding affinity has continued to increase. Thus, it is easy to create variations of an antibody once the target and application are identified. The patentee, having invested enormous sums in discovering the underlying target, has provided a blueprint for others who, now aware of the targets, can quickly make their own version of an effective antibody. The scope of the invention in this space is therefore the genus of antibodies that successfully binds the target, rather than any particular antibody that serves as an example.

Patent protection should be commensurate with that scope. Otherwise, the incentives to invest in new antibody therapies will disappear. Narrow protection places the targets and pathways in the hands of the public without the

corresponding reward of robust patent scope to their discoverers, who made considerable research and development investments. It allows after-arriving competitors and copyists to quickly (and much less expensively) appropriate the pioneers' research efforts.

As discussed below, the district court opinion on appeal essentially set forth a legal rule that would prevent a patentee from claiming a genus of antibodies unless the patentee has identified with certainty *each and every* possible antibody within the claims. This rule, if followed in cases going forward, would make it effectively impossible for innovator companies to obtain sufficiently broad patent protection. *See* Appx15; Appx23-24. Such a rule is also contrary to this Court's precedents. If affirmed, it will result in major prejudice to further innovation in the burgeoning field of molecular medicine, and ultimately harm patients.

SUMMARY OF THE ARGUMENT

This Court's decisions in *Angstadt*, *Wands*, and their progeny make clear that an antibody-genus claim is enabled so long as skilled artisans reading the patent, know how to make many antibodies and then screen them to isolate the antibodies with the desired function. *See In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *In re Angstadt*, 537 F.2d 498, 502-03 (C.C.P.A. 1976). Such methods of making and screening antibodies are routine in the art and have been for decades. Indeed, the evidence in this case showed that "the techniques for making

antibodies with [the] required binding properties were well-developed, automated, and routine." Amgen Br. 52; *see also id.* 33–34. Given that, it is irrelevant whether a Person of Ordinary skill in the Art (a POSA) can tell from a given antibody's amino-acid sequence, in the abstract, whether the antibody will have the required function. What matters is that the POSA knows how to make and use the claimed invention from the patent disclosure plus through routine and conventional methods.

The decision below reflects a fundamental misunderstanding of what is actually required to enable a POSA to practice antibody technologies. The district court disproportionately focused its analysis on the fact that the amino acid sequence of a given antibody does not necessarily predict its ability to bind to PCSK9. *See* Appx20 ("[T]here is no dispute that [the examples in the patent] 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 PCSK9 residues."). This approach ignores this Court's enablement precedents because it focuses primarily on unpredictability at the expense of other factors and focuses on the wrong kind of unpredictability to boot. This Court should not hold patentees of antibody technologies to such an impossibly high standard. Doing so would make it very difficult to obtain meaningful patent protection on antibody technologies and severely impede innovation in this field.

ARGUMENT

I. Enablement in antibody technologies requires that a POSA can follow the disclosure and practice the claims, which does not require predictability of the antibody's structure-function relationship.

In the so-called "unpredictable" arts like biotechnology, requiring accurate *prediction*—by definition—is a non-starter. Accordingly, courts do not assess enablement by determining whether a genus of molecular entities has a predictable structure-function relationship. Instead, courts ask whether the patent teaches a POSA how to generate molecular entities in the genus through routine methods and confirm that they have the required function through conventional testing and experimentation. If so, the genus is enabled.

The district court here asked the wrong question[1] and accordingly arrived at the wrong result. The uncertainty identified by the district court is present in *all*

[1] As explained in Amgen's brief, the district court's enablement analysis focused primarily on "something POSAs do not do: It asked whether POSAs can predict whether an antibody will bind to PCSK9 by looking at its amino-acid sequence alone." Amgen Br. 52. Having concluded that the answer to that question was no, the district court concluded that the patents were not enabled because the resulting unpredictability would require testing of antibodies to determine whether they have the claimed binding and blocking requirements. *See, e.g.*, Appx18 ("[S]ubstitutions 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."); Appx20 ("[T]here is no dispute that [the examples in the patent] 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 PCSK9 structures."); Appx25 ("[I]t is only through experimentation, not prediction that a [POSA] could conclude that a particular antibody would meet the binding and blocking requirements of the claim.") (citation omitted).

biological and chemical arts. If such unpredictability was allowed to control—i.e., if the standard were, "look at it and predict without testing"—then no genus claim in the life sciences would ever be valid. That is not the law.

A. *Angstadt* and its progeny control the enablement analysis here.

The Court's predecessor's decision in *Angstadt*—issued over 40 years ago—sets forth the applicable legal principles clearly. The patent at issue there claimed a method of catalytically oxidizing secondary or tertiary alkylaromatic hydrocarbons to form a reaction mixture comprising the corresponding hydroperoxides. *Angstadt*, 537 F.2d at 499. The PTO rejected the claims as not enabled because a skilled artisan reading the patent would not have known which catalysts would produce the desired hydroperoxides without testing them. *See id.* at 501.

The Court reversed. The patentee, the Court explained, was not required to "disclos[e] a test with every species covered by a claim" because that would necessitate a specification containing thousands of examples and would force the patentee "to carry out a prohibitive number of actual experiments." *Id.* at 502–03. Such a rule, in turn, would "discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed." *Id.* at 503. That analysis was then

clarified and followed in *Wands*. Neither case has been overruled, and the holdings in those cases control the outcome here.

1. *Angstadt* expressly rejected prediction as the measure of enablement.

The dissent in *Angstadt* argued that the claims were not enabled because a skilled artisan would not have known in advance which catalysts would work in producing hydroperoxides. *See id.* at 507 (Miller, J., dissenting). The majority soundly rejected that approach:

> If . . . the disclosure must provide "guidance which will enable one skilled in the art to determine, with *reasonable certainty* before performing the reaction, whether the claimed product will be obtained," as the dissent claims, then all "experimentation" is "undue," since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act, which is to encourage disclosure of inventions and thereby to promote progress in the useful arts. *To require disclosures in patent applications to transcend the level of knowledge of those skilled in the art would stifle the disclosure of inventions in fields man understands imperfectly*, like catalytic chemistry.

Id. at 503 (emphases added).

Yet that is exactly the approach that the district court adopted here. The court held that Amgen's claims were not enabled because the patent "do[es] not teach a person of ordinary skill in the art how to predict from an antibody's sequence whether it will bind to specific PCSK9 residues." Appx20. As *Angstadt* makes clear, that is not the test.

2. This Court's decision in *Wands* further mandates a finding of enablement here.

In *Wands*, this Court specifically applied *Angstadt*'s analysis of enablement of generic claims in the unpredictable arts to antibody technology. The claims in *Wands* were directed to (i) methods of assaying for HbsAg using monoclonal antibodies and (ii) the antibodies used in those assays. 858 F.2d at 734. It was undisputed that generating many monoclonal antibodies from hybridoma fusions was routine. *See id.* at 736.

Once made, the questions asked of the many antibodies so generated were three, each corresponding to a claim limitation: (1) Is the antibody an IgM? (2) Does it bind to HBsAg? and (3) Does it have an affinity greater than 10^{-9} M^{-1} ? *See id.* at 738. These questions were answered by three routine screening assays, no matter the uncertainty of predictions or the ultimate success rate. *Id.*[2] Since the assays were able to reliably identify embodiments of the claims, it did not matter *how many* antibodies fell within the claims and how many did not. The assays

[2] The Court in *Wands* had this to say about success rates in antibody screening assays: "Even if we were to accept the PTO's 2.8% success rate [in contrast to the success rate of 44% proposed by Wands], we would not be required to reach a conclusion of undue experimentation. Such a determination must be made in view of the circumstances of each case and cannot be made solely by reference to a particular numerical cutoff." *Wands*, 858 F.2d at 739 n.29.

provided the answers. *See id.* Accordingly, "undue experimentation would not be required to practice the invention," and Wands' claims were enabled. *Id.* at 740.

The same is true here. As the district court recognized, relying on Amgen's inventor's testimony, the techniques outlined in the patent at issue here allowed skilled artisans to (i) make antibodies that bind to PCSK9; (ii) screen those antibodies to determine which ones block interaction of PCSK9 with the LDL receptor; and then (iii) further screen the antibodies to determine which ones were strong blockers. Appx15. This evidence shows the "funnel" shape of the inquiry, just as in *Wands:* By routine testing, one goes from a pool of binding antibodies, to subset that block binding of the LDL receptor to PCSK9, to a smaller subset that are strong blockers. *See id.* This is identical to the questions asked in *Wands*.

It is undisputed that steps for making and screening antibodies were routine at the filing date. *See* Amgen Br. 14. It is undisputed that testing those by routine assays to evaluate which antibodies bind to PCSK9 was routine. *See id.* And it is undisputed that further testing the binders to see which ones bind to at least two of fifteen residues was routine. *See id.* at 14–15. Since it is undisputed that the binding assays were routine and reproducible, the success rate is irrelevant. The enablement analysis is therefore controlled by *Wands*.

In fact, the situation here is even more conducive to genus-claim enablement than it was in *Wands*. It is undisputed that the claimed antibodies here could be

identified through *automated* high-throughput techniques. Appx23. The district court dismissed this evidence on the basis that Amgen did not show that these techniques would be quick, cheap, and efficient. *Id.* But, even if that were true, it would be irrelevant to the question here: whether the amount of experimentation required would be "undue." *Wands*, 858 F.2d at 736. Experimentation that can be routinely conducted using automated methods cannot reasonably be characterized as "undue." As the *Wands* Court observed, "[t]he [undue experimentation] test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine." *Id.* at 737.

The district court summarily dismissed *Wands* in a footnote, stating that it deals with a "method patent," not a product one, as is the case with the claims here. Appx17 n.8. That is wrong. There were two claims in the *Wands* appeal drawn to products—claims 19 and 26. *See Wands*, 858 F.2d at 734, 741. The rest of the claims in *Wands* were immunoassay method claims. The enablement question concerned the scope of the genus of antibodies being used in the immunoassay. This Court reversed the PTO's enablement rejection for both sets of claims, products *and* methods, and the reasoning was the same for both. Indeed, this Court has routinely applied *Wands* to product claims in the years since it was decided. *See, e.g.*, *Enzo Biochem., Inc. v. Calgene, Inc.*, 188 F.3d 1362 (Fed. Cir. 1999) (plant cells); *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993) (vaccines); *In re Vaeck*,

947 F.2d 488 (Fed. Cir. 1991) (chimeric genes); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991) (DNA sequences).

While the district court used the eight *Wands* factors to analyze enablement, it failed to follow that case's fundamental holding: if a POSA can routinely make and screen antibodies to see which ones are within the claim and which are not, that is sufficient for enablement. *Wands*, 858 F.2d at 737. That holding controls this case.

B. Falsely equating iterative trial and error with undue experimentation undermines the progress of science and innovation.

Conditioning patentability of genus claims on the disclosure of so many species that iterative trial and error is eliminated is counterproductive and contrary to law. "To require such a complete disclosure," the *Angstadt* court explained, would "necessitate a patent application [] with 'thousands' of examples .... [S]uch a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments." 537 F.2d at 502-503.

The test for enablement is whether it would "require undue experimentation to obtain antibodies *needed to practice the claimed invention.*" *Wands*, 858 F.2d at 740 (emphasis added). The district court here did not ask that question. Instead, it observed that skilled artisans following the patent's roadmap might have to conduct "iterative trial and error," Appx22, and that there might be hypothetical

antibodies falling within the scope of the claims that a skilled artisan has not yet discovered. *See* Appx23. That is irrelevant. *Wands* itself rejected precisely this sort of analysis as "strained and unduly harsh." 858 F.2d at 739. What matters is that the patentees here enabled POSAs to make the antibodies in the claims' scope without undue experimentation. That satisfies the enablement requirement under this Court's precedents.

1. The disclosure in Amgen's patent provides a clear roadmap that eliminates undue experimentation.

The district court's error appeared to turn in large part on its conclusion that a POSA following the instructions set forth in the inventor's patent would have to engage in the same amount of experimentation as the inventor to discover antibodies *de novo*. Appx22–24. As demonstrated in Amgen's brief (at 61–63), that statement is incorrect as a matter of fact and irrelevant as a matter of law.

The inventors here discovered antibodies that block the binding of PCSK9 to the LDL receptor, thus providing therapy for hyperlipidemia. The inventors provided POSAs with a method of making candidate antibodies and instructed POSAs how to tell, by routine assays, which antibodies work and which do not. With the benefit of these disclosures, a POSA is able to easily test antibody sources by routine screening assays to find desired antibodies. *See Wands*, 858 F.2d at 740 ("[P]ractitioners of this art [monoclonal antibodies] are prepared to screen negative

hybridomas in order to find one that makes the desired antibody."). There is, after the act of invention, a clear roadmap for finding antibodies within the claims.

The Court's conclusion ignores the involved time, effort, and creativity that it took the inventors to come up with the concept in the first place, to test it again and again to make sure it is robust, and then to provide their roadmap to the world. That concept involved identifying the disease, associating it with the essential target, finding the "sweet spot" on the target to which the antibody should bind, and then screening for a few antibodies that effectively bind the target and thereby treat the disease. Once that is disclosed, all that is left for the world to do is to conduct routine testing to find the additional antibodies to the extent desired. That pales in comparison to the amount of experimentation required of the act of invention.

2. Requiring the rote disclosure of additional embodiments until trial and error is eliminated does not promote the progress of science.

It is the innovator's disclosure of the groundbreaking research and discovery of a new medicine—not the innovator's gratuitous padding of its patent disclosure—that the patent laws are meant to reward. When a disclosure contains sufficient instruction—whether through working examples or otherwise—for the ordinary artisan to make additional claimed embodiments, then § 112 is satisfied. *See Wands*, 858 F.2d at 740 (finding that undue experimentation does not turn on

the number of embodiments never screened). The requirement to have numerous examples will force researchers to expend time and resources on bulking up patent filings rather than innovating the next breakthrough treatment.

The district court's emphasis on predictability here echoes the rigid tests rejected in *KSR* and *Bilski*. *KSR Intern. Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007); *Bilski v. Kappos*, 561 U.S. 593, 604 (2010). Although disclosing several working examples may provide a helpful insight under certain facts, "[h]elpful insights . . . need not become rigid and mandatory formulas." *KSR*, 550 U.S. at 419. Enablement should not be converted from a flexible inquiry about the kind of experimentation a POSA would conduct in view of a particular disclosure into an unwinnable numbers game.

3. This Court's decisions in *Enzo*, *Wyeth*, and *Idenix* do not justify an erroneous result here.

Amici take no position here on whether this Court's decisions in *Enzo Life Sci., Inc. v. Roche Molecular Sys, Inc.*, 928 F.3d 1340 (Fed. Cir. 2019); and *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013) were correctly decided.[3] In any event, and for purposes of this brief, it does not matter because these cases can be distinguished. These cases are not relevant because they do not deal with the nature and tools of antibody science, but rather concern specific

[3] Amicus Merck is challenging the basis for those decisions in co-pending litigation before this Court.

issues related to synthetic organic molecules claimed by formulae. The effect of the disclosures and the amount of experimentation and predictability in antibody technology (as discussed *Wands*) is fundamentally different than in small-molecule technology.[4]

For instance, the claims in *Enzo* were drawn to *synthetically* produced labeled polynucleotides containing a modified nucleotide where there are several interacting variable embodiments, such as the nature of the base, the type of label, the type of linker used to attach the label, and the location of the labels within the polynucleotide. 928 F.3d at 1343–44. These possibilities resulted in an extremely large number of possible embodiments. *See id.* at 1346–47. This Court held that the specification failed to teach one of skill in the art which combinations will produce a polynucleotide that is hybridizable and detectable upon hybridization. *See id.* at 1347. Here, in contrast, the specification specifically instructs skilled artisans how to make antibodies and determine which antibodies have the claimed features using well-known methods that are routine in the antibody arts.

The claims in *Wyeth* similarly were directed to large numbers of *synthetic* rapamycin compounds, which a POSA would have to first synthesize and then

[4] The district court also cited, *Idenix Pharmaceuticals LLC v. Gilead Sciences, Inc.*, 2018 WL 922125 (D. Del. Feb. 16, 2018). Just as in *Enzo* and *Wyeth,* the claims in *Idenix* involved organic small molecules (nucleosides for the treatment of hepatitis C) claimed by structural formulae that a POSA would have to synthesize. *Id.* at *15. *Idenix* is thus not instructive on enablement of antibody genera.

screen. *See* 720 F.3d at 1385–86. Synthesizing the compounds in the first instance was a "complicated and lengthy" process, and even then, "one of ordinary skill would need to assay each of at least tens of thousands of candidates," a process that could take "weeks." *Id.* at 1386. That is nothing like the situation here, where the patentee provided a roadmap instructing POSAs exactly how to make antibodies already demonstrated to have the required properties and exactly how to use those antibodies to isolate additional antibodies with the claimed requirements. *See* Amgen Br. 13–16.

The district court here, quoting *Wyeth*, stated that there was "'no genuine dispute that it would [be] 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." Appx25 (quoting *Wyeth*, 720 F.3d at 1385) (first emphasis added; second emphasis and brackets by district court). The court's altered quotation misleadingly suggests that the rapamycins at issue in *Wyeth* are like *Angstadt*'s catalysts or *Wand*'s antibodies. They are not.

Rapamycins are organic molecules; antibodies are biological ones. Organic molecules are synthesized, and each variant molecule must be synthesized by a unique process based on its predetermined structure. Antibodies are generated by natural immunization processes that are not unique to each variant and do not require knowledge of the variant's structure. In other words, antibodies are

harvested, while synthetic organic molecules are built. The experimentation and development of antibody technology is front-loaded into the identification of the target, binding affinity, and therapeutic result. Once that information is disclosed, the development and screening of additional variants is routine. There is no need to design and "synthesize" additional variants, the way that a POSA would have to design and synthesize molecule species in *Enzo*, *Wyeth*, and *Idenix*. This Court should not apply the analysis of those cases to the present facts at the expense of applying the far more applicable analysis of *Angstadt* and *Wands*, which mirror the present facts.

To be clear, meeting the enablement requirement for a synthetic organic molecule as a class is not necessarily more difficult than for biologics as a class; each case needs to be judged on its own facts using the *Wands* factors. Moreover, other types of claim or claim elements, such as forms or formulations of a small molecule, may be readily enabled under *Wands* where the level of skill in the art supports that the generation of these embodiments is routine and conventional.

II. It is not required to disclose every species that falls within the scope of a claim in order to enable the claims' "full scope."

The Court below, citing *Magsil v. Hitachi*, 687 F.3d 1377 (Fed. Cir. 2012), concluded that the requirements of 35 USC § 112 necessitate enabling the "full scope" of a claim. Such formulation is not the law for antibody technologies such as the ones claimed in this case. For the claims here, *Angstadt* and *Wands*, rather

than *Magsil v. Hitachi*, 687 F.3d 1377 (Fed. Cir. 2012), provide the applicable standard for enablement.

The reason that *Magsil* is not applicable here is that *Magsil* involved open-ended claims with a very low threshold—a "change in the resistance level by at least 10%." *Id.* at 1379. The *Magsil* claim therefore covered "resistive changes from at least 10% up to infinity." *Id.* at 1382. The Court found this claim not enabled because the specification did not explain any way to achieve levels significantly above the 10% threshold. That is why the Court discussed the concept of "full scope" enablement in *Magsil*. *Magsil's* "full scope" enablement thus does not inform the analysis here, where the claims are not open-ended or in the case of one claim, claim 29, only nominally so (80-100%). It would be an error to extrapolate the holding in *Magsil* to very different types of claims, such as the ones here.

This Court made clear in *Angstadt* that, in the unpredictable arts, the patentee need not disclose every species covered by the claim. *See* 537 F.2d at 502. "To require such a complete disclosure," the Court explained, would require the patentee to disclose a prohibitive number of examples and force the patentee "to carry out a prohibitive number of actual experiments." *Id.* at 502-503. "This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which

are expressly disclosed." *Id.* The Court made the same point in *Wands*: the specification of an antibody patent need only allow skilled artisans "to obtain antibodies *needed to practice the claimed invention*." 858 F.2d at 740 (emphasis added); *accord Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1188 (Fed. Cir. 2014).[5] As demonstrated in Amgen's brief, the patents here satisfy that standard. No more is required.

CONCLUSION

The decision below, if allowed to stand, would make it far too difficult for pioneers of therapeutic antibodies to obtain sufficiently robust and reliable patent protection for their inventions. The district court divorced the statutory and precedential inquiry from the true nature of innovation in this field and thereby undermined innovators' ability to obtain generic protection. Innovators who discover and disclose new targets and pathways and a method of producing corresponding antibodies should receive, in exchange, the reward of sufficient patent protection. That is the fundamental quid pro quo of our patent laws.

The district court's approach would saddle these inventors with a virtually impossible task: reducing to practice and describing every single possible member of the claimed genus. This "would force an inventor seeking adequate patent

[5] To the extent the district court in *MorphoSys AG v. Janssen Biotech, Inc.*, 358 F. Supp. 3d 354 (D. Del. 2019) (cited at Appx12), suggested otherwise, it disregarded this Court's binding precedents.

protection to carry out a prohibitive number of actual experiments." *Angstadt*, 537 F.2d at 502-503. Such an exercise, carried out solely for patent purposes, diverts resources from supporting further innovation and deters entities from disclosing their inventions to the public. *See id.* at 504 ("Depriving inventors of claims which adequately protect them and limiting them to claims which practically invite appropriation of the invention while avoiding infringement inevitably has the effect of suppressing disclosure."). In effect, the district court's test gets the incentives exactly backwards: it encourages incremental advances, rather than fundamental ones.

The *Angstadt* majority's critique of the *Angstadt* dissent squarely applies to the district court's approach here: "The [district court] wants appellants to make everything predictable in advance, which is impracticable and unreasonable." *See id.* at 504. Absolute predictability is not and should not be required by the patent laws. The district court erred in concluding otherwise. For these reasons, amici curiae requests that this Court reverse the decision below.

Dated: February 28, 2020

Respectfully submitted,

/s/ Jorge A. Goldstein

Jorge A. Goldstein
Eldora L. Ellison
Kristina Caggiano Kelly
William H. Milliken

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 New York Avenue NW
Washington, DC 20005
Tel: (202) 371-2600
Fax: (202) 371-2540

Counsel for Amici Curiae Bristol-Myers Squibb Company and Merck Sharp & Dohme Corp.

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/s/ Kristina Caggiano Kelly
Signature of Counsel

Law Firm	Sterne, Kessler, Goldstein & Fox P.L.L.C.
Address	1100 New York Avenue, NW
City, State, Zip	Washington, DC 20005
Telephone Number	(202) 371-2600
Fax Number	(202) 371-2540
E-Mail Address	kckelly@sternekessler.com

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