2018-1691

United States Court of Appeals for the Federal Circuit

IDENIX PHARMACEUTICALS LLC and
UNIVERSITA DEGLI STUDI DI CAGLIARI,

Plaintiffs-Appellants,

– v. –

GILEAD SCIENCES INC.,

Defendant-Appellee.

On Appeal from the United States District Court for the District of Delaware in No. 1:14-cv-00846-LPS, Honorable Leonard P. Stark, Chief Judge

BRIEF OF *AMICI CURIAE* REGENXBIO INC. AND PROFESSOR HUGH C. HANSEN IN SUPPORT OF PETITION FOR REHEARING *EN BANC*

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JANUARY 29, 2020

CERTIFICATE OF INTEREST FOR *AMICI CURIAE*
REGENXBIO INC. AND PROFESSOR HUGH C. HANSEN

1. Full name of party represented by me:

   REGENXBIO Inc.

   Professor Hugh C. Hansen

2. Name of Real Party in interest (Please only include any real party in interest NOT identified in Question 3) represented by me is:

   None

3. Parent corporations and publicly held companies that own 10 percent or more of stock in the party:

   For REGENXBIO Inc.: BlackRock, Inc.

   For Professor Hugh C. Hansen: None

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

   None

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.

Dated: January 29, 2020

/s/ *Nicholas Groombridge*
Nicholas Groombridge

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STATEMENT OF INTEREST OF *AMICI CURIAE*

REGENXBIO Inc. ("REGENXBIO") is a clinical-stage biotechnology company seeking to improve lives through the curative potential of gene therapy.[1] Professor Hugh C. Hansen has more than 40 years of intellectual property law experience. *Amici* REGENXBIO and Professor Hansen, who have no stake in this case, support Appellants' Petition For Rehearing *En Banc* because the panel's decision in *Idenix Pharmaceuticals LLC* v. *Gilead Sciences Inc*., 941 F.3d 1149 (Fed. Cir. 2019), threatens to foreclose adequate patent protection for groundbreaking gene therapies.

Millions of people are affected by genetic changes—mutations or deletions in their DNA—or other metabolic dysfunctions that adversely impact their health. They face chronic disease and require expensive medications to control their symptoms. Gene therapy offers a revolutionary alternative: a chance to treat the underlying cause of the disease—by introducing a therapeutic gene that corrects the course of disease—and potentially provide lasting results from a single therapeutic dose.

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[1] All parties have consented to the filing of this *amicus* brief. Pursuant to Federal Circuit Rule 35(g), a motion for leave to file is submitted with this brief.

No party's counsel authored this brief in whole or in part. No party, party's counsel, nor any person other than *amici curiae* contributed money that was intended to fund preparing or submitting this brief.

Gene therapy uses a "vector" to transport therapeutic DNA into the body's cells. REGENXBIO has exclusive rights to innovative viral vectors developed at the University of Pennsylvania, known as NAV® Vectors, to treat genetic defects or supply therapeutic factors such as antibodies to treat other serious conditions. Upon administration to a patient, the vectors deliver functional genes to the nucleus of affected cells. Once there, they serve as a genetic blueprint, supplying the function needed to treat or cure the disease.

REGENXBIO focuses on diseases with significant unmet needs, such as retinal, metabolic, and neurodegenerative diseases. As a key aspect of its business, REGENXBIO also licenses the patented NAV® Vector technology to other companies developing their own gene therapies.

Like many other biotechnology companies, REGENXBIO relies on the patent system to protect its inventions. Patents are critical to such businesses and their ability to fund future research.

Professor Hansen is the director of the Emily C. and John E. Hansen Intellectual Property Law Institute at Fordham Law School. He is also the founder of the Annual Fordham Intellectual Property Law and Policy Conference. Professor Hansen shares REGENXBIO's concern regarding the panel's departure from precedent and the impact the panel's decision will have on emerging technologies, including gene therapy.

ARGUMENT

I. The Panel's Decision Imposes Section 112 Requirements That Would Thwart Protection For Groundbreaking Inventions

The patent at issue in *Idenix*, U.S. Patent No. 7,608,597, claims a method of treatment using a structurally defined chemical genus of β-D-2′-methyl-ribofuranosyl nucleosides. *Idenix*, 941 F.3d at 1155. While acknowledging that the patent disclosed thousands of compounds within the recited genus, *id*. at 1158, the panel invalidated the claims under 35 U.S.C. §112, based on the absence of disclosure of a single species—the accused product. In effect, the panel judged compliance with the written description and enablement requirements not on the basis of the patent's disclosure itself, but rather on what it did not disclose about the accused product. It is untenable that patent validity under Section 112 should depend on an infringer's activity, rather than on the robustness of the patent disclosure. Taken to extremes, the panel's reasoning would lead to the illogical result that a patent could be found valid under Section 112 against one infringer yet, based on its same disclosure, invalid against another.

Of concern, the panel's reasoning may not be confined to pharmaceutical-chemistry inventions, and may instead extend to other technologies, including biologics and DNA-based inventions of great importance in advancing gene therapy.

Indeed, the panel's decision is especially troubling for DNA-based inventions. Forty years ago, the Supreme Court took an expansive view of the patentability of

DNA-based inventions. *See Diamond* v. *Chakrabarty*, 447 U.S. 303, 305, 318 (1980). That decision permitted and protected the explosive growth of the domestic biotechnology industry in the 1980's. Subsequent decisions, however, have made it more difficult to obtain, and have even eliminated, patent protection for DNA-based inventions. For example, this Court has held there can be no conception of a DNA invention without actual reduction to practice where an inventor is unable to envision the DNA's "constitution" in a distinguishing way, *see Amgen, Inc.* v. *Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991), and that a genus of DNAs can be described only through disclosure of a still undefined "representative number" of species, *see Regents of the Univ. of California* v. *Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997). And the Supreme Court held that isolated naturally occurring DNA sequences cannot be patented at all. *See Ass'n for Molecular Pathology* v. *Myriad Genetics, Inc.*, 569 U.S. 576, 591-92 (2013).

The panel's decision goes even further, placing unreasonable demands on method of treatment claims that recite the therapeutic agent as a genus. *Idenix* could be read to require disclosure of the accused infringing product in order to support a genus that includes that product, *see Idenix*, 941 F.3d at 1165, and to measure enablement not by whether the experimentation needed to make and test particular embodied species is "undue," but by how long it would take a skilled artisan to make

and test each species within the genus—even if that work would be routine. *See id.* at 1162-63.

The panel's decision may be interpreted to have heightened the written description and enablement requirements in ways that are unwarranted by science, precedent, or policy, and that threaten some of the most needed inventions. The *en banc* Court should intervene before the panel's reasoning frustrates patent protection across the innovative landscape.

II. Written Description Support For A Genus Should Not Require Disclosure Of The Accused Infringing Product

The written description requirement should focus on the patent itself. It "'requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art.'" *Id*. at 1163 (quoting *Ariad Pharm., Inc.* v. *Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (*en banc*)). Recent case law though reveals a drift away from this longstanding proposition, and the panel's decision threatens to accelerate this trend exponentially.

In *Abbvie Deutschland GmbH & Co*. v. *Janssen Biotech, Inc*., 759 F.3d 1285, 1300-01 (Fed. Cir. 2014), this Court looked at the accused product in order to understand which species fell within the scope of the claimed genus. The Court concluded that each of the 300 exemplary antibodies in the specification were "all of [a] similar type," and did "not qualitatively represent other types of antibodies encompassed by the genus." *Id*. at 1300. The Court acknowledged that the patents-

in-suit "need not describe the allegedly infringing [antibody] in exact terms," but held that the patents "must at least describe some species representative of antibodies that are structurally similar to" the accused product. *Id*. at 1301.

The panel's opinion does not cite *AbbVie*, but takes consideration of an accused product far beyond *AbbVie*'s holding. The panel rejected *AbbVie*'s view that disclosure of compounds structurally similar to the accused product—those containing "other halogens"—was sufficient. *Idenix*, 941 F.3d at 1165. To the contrary, it relied on the "conspicuous[] absence" of the exact halogen used in the infringing product—fluorine—to find the claims invalid for lack of written description. *Id*. The panel's decision will likely be read as making the absence of a single species from the specification dispositive of whether an otherwise-supported genus claim meets the written description requirement.

The panel relied on *Ariad* for the proposition that the written description requirement defends "against attempts to 'cover any compound later actually invented and determined to fall within the claim's functional boundaries.'" *Id*. at 1164-65 (quoting *Ariad*, 598 F.3d at 1353) (emphasis added). But that policy rationale, critically important as it is, cannot bear the weight the panel placed on it. The claims at issue in *Ariad* were phrased in purely functional language, with few if any disclosed species actually exhibiting that function. *Ariad*, 598 F.3d at 1340-41, 1350. Here, in contrast, the claims recite a genus identified not only by function but

by chemical formula. *See Idenix*, 941 F.3d at 1155. The panel recognized that the specification disclosed numerous species, by structure, within that genus. *See id*. at 1157-58. Indeed, the panel stated that the '597 patent "provides adequate written description for the compounds within its formulas." *Id*. at 1164. But the panel held that "the listed examples and formulas cannot provide adequate written description support for undisclosed nucleosides that also happen to treat [Hepatitis C]." *Id*. (emphasis added).

The panel's decision will be read to invalidate genus claims that do not identify every species within the genus, or at least that do not happen to identify the species represented by the accused product. That is not, and should not be, the correct written description analysis. The proper analysis is whether the specification describes, or evidences possession of, the genus, not whether it happens to call out the accused product itself as a species. Under the panel's approach, whether a patent has adequate written description will turn, in part, on the happenstance of which species competitors develop into marketed products. That, in turn, incentivizes competitors to use the patent's disclosure as a guide to develop undisclosed species, knowing that finding one will allow them to avoid infringement by sounding the death knell for the patent on which they relied. This cannot be right. This Court's predecessor recognized that "[d]epriving inventors of claims which adequately protect them and limiting them to claims which practically invite appropriation of

the invention while avoiding infringement has the effect of suppressing disclosure." *In re Angstadt*, 537 F.2d 498, 504 (C.C.P.A. 1976). Moreover, the panel's approach to written description distances the written description requirement for validity from that used to obtain a patent; the Patent Office (properly) judges written description by looking within the application's four corners, and not at any known or contemplated accused products.

Here, the Patent Office found the disclosure of the patent adequate; a jury found the disclosure of the patent adequate; and the district court left the jury's finding undisturbed. This Court should review the panel's decision *en banc*, restore the jury's verdict, and restore the law of written description.

III. Enablement Of A Genus With Biological Function Should Not Be A Numbers Game

This Court has long held that claims are enabled where the patent allows a person of ordinary skill to make and use the claimed invention without "undue" experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). However, the *Idenix* finding of no enablement rested almost exclusively on a mathematical calculation of the size of a chemical genus and the time it would take to synthesize and screen each compound within it for activity against Hepatitis C. Indeed, despite finding that the methods needed to synthesize and to screen the claimed compounds were "routine," the panel found the claims not enabled because of the time required

to carry out those activities for each member of the claimed genus. *Idenix*, 941 F.3d at 1158-60.

Idenix suggests that for enablement, the size of a claimed genus and the time it would take to make and test its members is now determinative, regardless of whether that experimentation is actually undue. Enablement, however, should not be a mere numbers game. This is especially true in fields where, with robotics and high throughput screening techniques, millions of compounds can be made and tested in relatively short order. Section 112, first paragraph, requires a patent to enable a skilled artisan to practice any embodiment of the claim without undue experimentation. Thus, the proper inquiry for compliance is whether each individual embodiment is enabled. The proper inquiry is not how long it would take one skilled artisan to make all of the embodiments of a claim. No skilled artisan would ever do that. And by focusing on the size of the genus, the panel's analysis would invalidate large genera even where a skilled artisan could make and test each individual species with ease.

In reaching its decision, the panel relied on *Wyeth & Cordis Corp.* v. *Abbott Labs.*, 720 F.3d 1380, 1386 (Fed. Cir. 2013), which found that the need to engage in a "systematic screening process" for each potential compound in the claimed genus was "excessive" and thus undue. But in *Wyeth* the need for systematic screening resulted from the fact that the claim term "rapamycin" represented a poorly

understood genus of extremely chemically complex natural compounds made by the bacterium *Streptomyces hygroscopicus*, yet only a single rapamycin species was disclosed. *Id*. at 1382.

In contrast, here, the numerous disclosed compounds within the claimed genus, all purine and pyrimidine nucleosides, can be made by routine chemical synthesis and tested by routine assays. *Idenix*, 941 F.3d at 1160. No experimentation was undue, as in *Wyeth*. The panel nevertheless focused on the unremarkable possibility that not every compound within the claimed genus would have efficacy in treating Hepatitis C. *Id*. at 1159. But the law allows claims to encompass inoperative embodiments. *See Atlas Powder Co.* v. *E.I. Du Pont De Nemours & Co.*, 750 F.2d 1569, 1576-77 (Fed. Cir. 1984). And, as this Court has repeatedly held, experimentation is not undue merely because it is extensive. *See Cephalon, Inc.* v. *Watson Pharms., Inc.*, 707 F.3d 1330, 1338-39 (Fed. Cir. 2013) ("[E]xtensive experimentation does not necessarily render the experiments unduly extensive where the experiments involve repetition of known or commonly used techniques…. Thus, the 'focus is not merely quantitative …'") (quoting *PPG Indus., Inc.* v. *Guardian Indus. Corp*., 75 F.3d 1558, 1564 (Fed. Cir. 1996)).

The Court should grant *en banc* review to correct the grave errors made by the panel in judging enablement of a method of treatment claim reciting a structurally

identified chemical genus that did not require undue experimentation to make and use.

IV. Unpredictable Section 112 Law Disproportionately Harms Start-Ups

The panel's opinion creates significant new uncertainties for companies like REGENXBIO seeking to protect their groundbreaking technology. Following *Idenix*, patentees are left to guess how many experiments they must perform to support their claims to a genus. And they must worry that no matter how many experiments they perform and how many species they disclose, their patent may someday fall if a competitor—motivated by *Idenix*—commercializes an undisclosed species unquestionably within the genus. If the panel's view of Section 112 controls, companies will have to waste valuable resources doing experiments for patents, not patients. *See In re Angstadt*, 537 F.2d at 502-03 (explaining "require[ing] disclosure of a test with every species covered by a claim" 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").

Start-ups and small companies would bear a disproportionate burden in such a system. Those companies cannot forego patent protection. But if they have to divert scant resources to multiplicative experiments to support a genus-scope claim, new therapies will go undiscovered. That rule of law serves neither innovators nor the public as a whole.

CONCLUSION

For the foregoing reasons, *amici* respectfully request that the Court grant rehearing *en banc* to address these issues.

Dated: January 29, 2020

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

Pursuant to Federal Rule of Appellate Procedure 32(g), this brief complies with the type-volume limitation of Federal Rule of Appellate Procedure 32(a) and 29(b)(4) and of Federal Circuit Rule 35(g). The brief contains 2,568 words, excluding parts of the brief exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b). The word count includes the words counted by the Microsoft Word 2016 function and the words counted in the images.

This brief also complies with the typeface requirements of Federal Rule of Appellate Procedure 32(a)(5) and the type style requirements of Federal Rule of Appellate Procedure 32(a)(6). The brief has been prepared in a proportionally spaced typeface using Microsoft Word 2010 in 14-point font of Times New Roman.

Dated: January 29, 2020

/s/ *Nicholas Groombridge*
Nicholas Groombridge

CERTIFICATE OF SERVICE

The undersigned hereby certifies that on this 29th day of January 2020, the foregoing BRIEF OF *AMICI CURIAE* REGENXBIO INC. AND PROFESSOR HUGH C. HANSEN IN SUPPORT OF PETITION FOR REHEARING *EN BANC* was filed electronically with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the Court's CM/ECF system.

Dated: January 29, 2020

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