No. 19-1133

In the United States Court of Appeals for the Federal Circuit

BIOGEN MA, INC.,
Plaintiff-Appellee

v.

EMD SERONO, INC.,
PFIZER INC.,
Defendants-Appellants,

BAYER HEALTHCARE PHARMACEUTICALS INC.,
NOVARTIS PHARMACEUTICALS CORP.,
Defendants.

On Appeal from the United States District Court
for the District of New Jersey
(Civ. No. 10-2734) (The Honorable Claire C. Cecchi, J.)

BRIEF OF AMICUS CURIAE BAYER HEALTHCARE PHARMACEUTICALS INC. IN SUPPORT OF DEFENDANTS-APPELLANTS

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CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, undersigned counsel for amicus curiae certifies the following:

1. The full name of the amicus represented by me in this case is Bayer HealthCare Pharmaceuticals Inc.

2. The name of the real party in interest represented by me is the same.

3. Bayer HealthCare Pharmaceuticals Inc. is indirectly wholly owned by Bayer AG, a publicly traded company. Information about Bayer AG's ownership structure is reported at:

http://www.investor.bayer.com/en/stock/ownership-structure/.

4. The names of all law firms and the partners and associates that have appeared for the party in the lower tribunal or are expected to appear for the party in this court and who are not already listed on the docket for the current case are:

(a) George A. Borden, Thomas S. Fletcher, Kyle E. Thomason, and Tian Huang, all of Williams & Connolly LLP, 725 Twelfth Street, N.W., Washington, DC 20005;

(b) Jamie Simpson, Hannah Stott-Bumsted, Eric Wiener, and Marta

Chlistunoff, all formerly of Williams & Connolly LLP, 725 Twelfth Street, N.W., Washington, DC 20005; and

(c) Robert M. Goodman, C. Brian Kornbrek, and Thomas K. Murphy III, all of Greenbaum, Rowe, Smith & Davis LLP, 75 Livingston Avenue, Suite 301, Roseland, New Jersey 07068.

5. This Court's decision in the pending appeal will directly affect the following case that is currently pending in the United States District Court for the District of New Jersey: *Bayer HealthCare Pharmaceuticals Inc. v. Biogen MA, Inc.*, Civ. No. 10-2734 (Hon. Claire C. Cecchi, J.).

/s/ Bruce R. Genderson
BRUCE R. GENDERSON

Attorney for Bayer HealthCare Pharmaceuticals Inc.

APRIL 15, 2019

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Bayer HealthCare Pharmaceuticals Inc. ("Bayer") submits this brief as amicus curiae pursuant to Rule 29 of the Federal Rules of Appellate Procedure and this Court's Rule 29.

INTEREST OF THE AMICUS CURIAE

Bayer is a research pharmaceutical company that discovers, develops, and markets innovative medicines. It makes and sells Betaseron®, which won FDA approval in 1993 and became the first disease-modifying therapy for multiple sclerosis in the United States. The active ingredient in Betaseron® is a "mutein"—i.e., a genetically engineered variant of—the naturally occurring human protein interferon-β ("IFN-β"). Betaseron®'s active ingredient is produced recombinantly in *E. coli* bacterial cells.

Bayer's interest in this appeal is that Plaintiff Biogen MA, Inc. ("Biogen") also alleges that the use of Betaseron® infringes claim 1 of U.S. Patent No. 7,588,755 (the "Fiers Patent"), the patent at issue in the appeal. Biogen sued Bayer as well as Defendants-Appellants EMD Serono, Inc. and Pfizer, Inc. in the same complaint, and the case proceeded as a single action through fact and expert discovery and summary judgment briefing. The district court then severed the claims against Bayer from those against Serono and Pfizer, and it ordered the claims against Serono and Pfizer to be tried first. Bayer

expects its case to proceed if claim 1 of the Fiers Patent is not invalidated or deemed ineligible.

Pursuant to Fed. R. App. P. 29(a)(4), amicus curiae states that no party or counsel for any party to this appeal authored this brief in whole or in part, and no person other than amicus curiae or its counsel contributed money toward the preparation or submission of this brief.

SUMMARY OF ARGUMENT

In the late 1970s into early 1980, researchers around the world were racing to find a way to use genetic-engineering technology to produce IFN-β, an antiviral protein made naturally by the human body. Other scientists had already shown that natural IFN-β, isolated from human cells, could be used to treat various diseases. The race concluded in early 1980, but the winner was not Dr. Walter Fiers, the named inventor of the patent in suit here. Following a lengthy interference proceeding, this Court determined that a group led by Dr. Tadatsugu Taniguchi was the first to discover the DNA sequence of IFN-β. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). Dr. Fiers also did not

invent recombinant IFN-β itself. *See Biogen MA, Inc. v. Japanese Foundation for Cancer Research*, 785 F.3d 648 (Fed. Cir. 2015).[1] Nonetheless, after nearly 30 years of prosecution, the Patent Office issued a patent to Dr. Fiers for the use of recombinant IFN-β "polypeptides" to treat various diseases, despite the fact that he treated no one and admittedly added nothing to the prior art as to treatment.

The Fiers Patent is clearly invalid, as Appellants' brief persuasively establishes. Indeed, under the patent's controlling definition of "polypeptide," the district court's JMOL ruling cannot stand. As amicus curiae, Bayer adds additional perspective that Appellants do not cover. First, we explain why the law requires that a new process of making a product must impart *both* structural and functional differences from prior-art products to impart novelty—a point Appellants have no reason to emphasize, in light of their clear proof at trial that Dr. Fiers's process of making recombinant IFN-β imparted neither structural nor functional differences from the native human IFN-β of the prior

[1] In an interference between Dr. Fiers and Dr. Taniguchi's group, the Patent Trial and Appeal Board stated that in light of the known IFN-β "DNA and the known genetic code indicating which DNA sequences encode each amino acid, those of skill in the art would have considered the polypeptide Fiers now claims to have been obvious." The Board held that Biogen failed to overcome this conclusion, and this Court affirmed. *Biogen MA, Inc.*, 785 F.3d 648.

art. Next, we explain that the district court erred as a matter of law by relying on the asserted efficiency advantages of Dr. Fiers's *process* as a functional difference in the resulting *product* of that process. Finally, we address the potential implications of the Court's decision for an important issue in Biogen's pending infringement action against Bayer—the astonishing overbreadth of the genus of muteins of claim 1 of the Fiers Patent, which dooms it to fail the written description requirement of 35 U.S.C. § 112. This issue is intertwined with the Section 112 issues Appellants raise, but goes beyond them.

ARGUMENT

I. The JMOL Should Be Reversed and the Jury's Finding that the Fiers Patent Is Anticipated by Prior-Art Treatment References Should Be Reinstated.

A. A Substance Must Be *Both* Structurally and Functionally Different To Be New.

It is bedrock law that an old use of an old product is not patentable. *See, e.g.*, *Providence Rubber Co. v. Goodyear*, 76 U.S. 788, 796 (1869). Here, because it is beyond dispute that Dr. Fiers added nothing to the prior art concerning treatment, the only question is whether the product his method of treatment employs was new or old.

The starting point of the correct analysis is the case law, dating back more than a century, holding that "[w]hile a new process for producing [a product] [is] patentable, the product itself [cannot] be patented, even though it was a product made artificially for the first time." *Cochrane v. Badische Anilin & Soda Fabrik ("BASF")*, 111 U.S. 293, 311 (1884); *see also Gen. Elec. Co. v. Wabash Appliance Corp.*, 304 U.S. 364, 373 (1938) ("[A] patentee who does not distinguish his product from what is old except by reference . . . to the process by which he produced it, cannot secure a monopoly on the product by whatever means produced.").

The development of biotechnology, including recombinant DNA technology, has provided occasion for this Court to revisit and apply these bedrock precedents. As with the novel synthetic method at issue in *BASF*, the biotechnology field often employs complex methods to produce products that perform the same functions as substances that are produced naturally. If these methods of production are novel and advantageous, they are clearly patentable. Dr. Fiers evidently was seeking a patent on a new method of production when he filed his application entitled "DNA Sequences, Recombinant DNA Molecules, and Processes for Producing Human Fibroblast Interferon-like Polypeptides." Appx99, Appx120 (col. 6, ll. 54-59). But Dr. Fiers did not succeed in

patenting any process for making anything. And because the Fiers Patent teaches no new method of treatment, Biogen's position now turns on the novelty of a product which is intended to be—and is—functionally identical to native human IFN-β. This Court's case law applying the longstanding principles cited above in this new context make clear that unless the process of making Dr. Fiers's polypeptides imparts *both* structural and functional differences from the native IFN-β of the prior art, they are not novel. Even if a product made by a new process bears in its structure some discernible fingerprint of that new process, the law does not recognize the product itself as "new," or as independently patentable, unless the structural differences matter to how the product functions.

This Court's decision in *Amgen Inc. v. F. Hoffmann-La Roche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), illustrates how this Court's established law of novelty applies in the recombinant-DNA context. That case involved Amgen's patents claiming various aspects of the recombinant protein erythropoietin ("EPO"). EPO is a naturally occurring protein that stimulates the production of red blood cells and is therefore useful in treating certain blood disorders. *Id.* at 1346. The prior-art method for obtaining EPO for therapeutic use was to isolate it from urine. *Id.* at 1347. "One critical distinction between EPO

extracted from urine and synthetically engineered EPO is that the urinary EPO has been exposed to enzymes and bodily processes that may hinder its efficacy for future use." *Amgen, Inc. v. F. Hoffmann-LaRoche Ltd.*, 581 F. Supp. 2d 160, 194 (D. Mass. 2008).[2] The evidence showed that the urinary EPO used in the prior-art therapeutic study "was not working properly" and that it "cleared quickly from the body and broke down in fragments." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 579 F. Supp. 2d 199, 209 (D. Mass. 2008). The scientist who authored the prior-art reference (Goldwasser) concluded that his attempt to use urinary EPO therapeutically was "a failure." *Id.* at 203.

In contrast to the failed prior-art use of urinary EPO, the results of the first clinical trials with Amgen's recombinant EPO were "dramatic beyond anyone's dreams." *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69, 116 (D. Mass. 2001).[3] Amgen asserted its patents against Roche. Roche argued that the claims were anticipated by the Goldwasser reference disclosing EPO isolated from urine.

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[2] *Aff'd in part and vacated in part*, *Amgen*, 580 F.3d 1340.

[3] *Aff'd in part, rev'd in part, vacated in part*, *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 457 F.3d 1293 (Fed. Cir. 2006).

After Amgen prevailed at trial, this Court considered "whether the production of EPO by recombinant technology resulted in a new product, so that claim 1 was not anticipated by the urinary EPO" in the prior art. 580 F.3d at 1367. The Court looked to the specification of the Amgen patent, which (unlike the specification of the Fiers Patent) cited studies detailing the functional differences between the recombinant EPO recited in the claims and the prior-art urinary EPO. *Id.* For example, the recombinant EPO and urinary EPO had different specific activity and stability in the human body. *Id.* at 1364. The Court concluded that Roche failed to prove that "recombinant EPO was the same as urinary EPO" because "urinary EPO and recombinant EPO were *structurally and functionally different.*" *Id.* (emphasis added). The Court did not merely analyze whether there were structural differences, nor did it consider the fact that the prior-art product was not recombinant to be dispositive, but rather went on to analyze and emphasize the meaningful difference in how the recombinant EPO functioned as a treatment.

Since *Amgen*, this Court has repeatedly endorsed and applied the principle that a source or process limitation cannot differentiate a claimed product from the prior art unless the limitation imparts "structural *and* functional differences distinguishing the claimed product from the prior art." *Greenliant*

Sys., Inc. v. Xicor LLC, 692 F.3d 1261, 1268 (Fed. Cir. 2012) (quoting *Amgen*, 580 F.3d at 1370) (emphasis added). *Greenliant* involved a patentee's attempt to recapture additional scope for his product-by-process claims under 35 U.S.C. § 251. This Court analyzed whether the patentee had surrendered the relevant subject matter—the use of reactants other than "TEOS" in his process—to "overcome prior art and secure the patent." *Id.* at 1267 (internal quotation marks omitted). The Court noted that the patentee had emphasized, to the patent examiner and in the Board of Patent Appeals and Interferences, not only structural but also functional differences between TEOS and other reactants: He had argued that the use of TEOS made the claimed devices "clearly different *and superior* to the prior art," and that "the prior art di[d] not possess *the characteristics* and structure" of the claimed device. 692 F.3d at 1269-70 (listing purported functional benefits of TEOS, including increased total charge that could be conducted, less tensile stress and thus longer useful life, and fewer pinhole defects). That the patentee argued these functional differences, and that this Court found them significant in assessing whether the patentee's arguments were "to overcome prior art," reflects once again that mere physical differences, without functional impact, would not have sufficed to distinguish the patentee's devices from the prior-art devices.

In *Purdue Pharma L.P. v. Epic Pharma, LLC*, 811 F.3d 1345 (Fed. Cir. 2016), this Court yet again reiterated the rule of *Amgen* that "structural *and* functional differences" are required to distinguish a claimed product from the prior art. *Id.* at 1354 (emphasis added) (internal quotation marks omitted). There, the Court held that the patentee had failed to show either structural or functional differences. *Id.*

District courts also have recognized and applied the *Amgen* standard. The court in *Cubist Pharmaceuticals, Inc. v. Hospira, Inc.*, 75 F. Supp. 3d 641 (D. Del. 2014), acknowledged that the law requires the claimed composition to "be structurally and functionally different from [prior art] compositions," *id.* at 669, and it applied this principle to facts on all fours with this case. Cubist's patent claimed "compositions having at least 93% pure daptomycin" purified by a particular process. *Id.* at 668. Hospira argued that a prior-art patent that disclosed a different method of purifying daptomycin anticipated Cubist's claim. Hospira did not dispute, and the court recognized, that the source limitation of Cubist's patent "result[ed] in the elimination of two types of impurities," which Cubist argued made the claim's composition "structurally differ-

ent." *Id.* at 668-69. The court nevertheless ruled that the claim was anticipated, because it accepted Hospira's argument that there were no "true functional differences" between the claimed product and the prior art. *Id.*

In this case, the district court incorrectly concluded that *Amgen* and its progeny are inapplicable because those cases involved product-by-process claims, while the Fiers Patent claims a method of using a genus of products. Appx33-36. That is not the law. A source limitation cannot make something novel unless it imparts structural and functional differences, no matter whether it is claimed as a product or as a method of using the product.

The Supreme Court's decision in *Leggett v. Standard Oil Co.*, 149 U.S. 287 (1893), is instructive and controlling on this point. That case involved a claim to a method of "coating or lining the inside of barrels" using glue that was obtained by a new process. In the prior art, glue for coating barrels had been "produced by reduction from a previously solid state," while in the claimed method the glue was "permitted to attain only a certain liquid consistency." 149 U.S. at 289-90. The Supreme Court addressed the precise question of whether a claim to an old use (coating barrels, analogous to treating viruses here) of a product functionally similar to a prior-art product (glue,

analogous to IFN-β here) made by a new process (produced by obtaining a liquid consistency, analogous to recombinant production here) can be novel.

The answer, of course, was no. The crucial inquiry was whether the product—obtained a different way—was structurally and functionally different, such "that barrels so 'glued' [using the patent's process of obtaining glue] are any *better* than those coated by the old process." *Id.* at 293 (emphasis added). The record "show[ed] that barrels lined under either the old or the new process are practically indistinguishable." *Id.* Accordingly, the "prior use and sale of liquid glue," prepared by a different process, "for various purposes, including that of coating barrels," "clearly anticipated" the claim. *Id.* at 295. It made no difference to this outcome that the claims at issue were directed to methods of using glue rather than to the glue. The same reasoning applies in this case: The prior-art administration of functionally identical native IFN-β clearly anticipates the Fiers Patent's claimed method of treatment.[4]

[4] The district court attempted to distinguish *Leggett* but misunderstood how its facts apply here. The court referred to the claimed method of coating as "the identical process [that] had been practiced in the prior art" (Appx34), but the relevant process for purposes of comparison to this case was the process implied by the claim's source limitation—the process of obtaining the glue, which corresponds to the process of recombinant production here. *Leggett* is therefore an example of product-by-process principles applying to a source limitation even though the claim is to a method of use of the product. Indeed, if the only question is whether the claimed method of administration

The district court also erred in holding that, even if product-by-process law applies, the law requires only structural differences. The court misunderstood this Court's teaching in *Amgen*. It erroneously stated that the *Amgen* court "made no mention of functional differences in affirming the anticipation rulings." Appx31. In fact, this Court made clear that "Roche did not meet its burden" to prove anticipation precisely "because urinary EPO and recombinant EPO were structurally *and functionally* different." 580 F.3d at 1370 (emphasis added). The district court also cited a section of the MPEP, but the MPEP does not bind this Court. *See, e.g., EmeraChem Holdings, LLC v. Volkswagen Group of America, Inc.*, 859 F.3d 1341, 1348 n.2 (Fed. Cir. 2017). In any event, the cited section provides only that "[t]he structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art," Appx32-33, not that functionality is irrelevant. Similarly, the treatise cited by the district court says only that structural differences are necessary to impart novelty ("the product still

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is the same as a prior-art method, then the Fiers Patent indisputably is anticipated, since Biogen concedes that Fiers added nothing to the prior-art methods of administration.

must be new in structural terms in order to meet the novelty requirement"), not that they are sufficient to do so. Appx33.

B. There Was Substantial Evidence of Both Structural and Functional Identicality, and Ease of Production Is Not a Functional Characteristic of a Product.

As discussed in Appellants' brief (at 16-18), Appellants presented substantial evidence that recombinant IFN-β and native IFN-β are both structurally and functionally identical. That is true whether or not this Court enforces the specification's definition of "polypeptide."

First, this Court should enforce the specification's definition that a "polypeptide" is a "linear array of amino acids." *Intervet Inc. v. Merial Ltd.*, 617 F.3d 1282, 1296 (Fed. Cir. 2010). Biogen agreed to the definition during claim-construction briefing in 2011 and it had nearly five years—until the district court eventually issued its claim-construction ruling as to the sole disputed issue in March 2016—to consider whether it wanted to alter the definition. It never even attempted to do so. Under that definition, there is no dispute that the patent is anticipated, since Biogen concedes that native IFN-β has the same linear array of amino acids as Appellants' product. *See* Appx25331 ("The sequential order of the amino acid residues for native IFN-β is the same as the sequential order of the amino acid residues for recombinant IFN-β.").

But even under the district court's incorrect post-verdict analysis, which looked beyond the amino-acid sequence to determine the relevant "structure" of the polypeptide, Appellants' brief amply demonstrates that there was substantial evidence not only that the structures of recombinant and prior-art native IFN-β are the same, but also that the *functions* are the same.

The district court erred in concluding that the fact that "recombinant interferon-β can be made in much larger quantities and much more easily than native, human interferon-β can be obtained" amounted to a functional difference. Appx30. That more IFN-β may be obtained using a recombinant process than the prior-art process of isolating IFN-β from natural sources is a difference and advantage of the process or source. It is not, however, a functional difference in the IFN-β itself. It is the IFN-β "polypeptide" that must be functionally distinct, not the process by which it is prepared, in order to avoid a finding of anticipation. The law has been clear and consistent for nearly 150 years: An improved process for preparing a composition is not—and never has been—enough to impart novelty to the composition. In *BASF*, the artificial source of the claim "made it possible to obtain the alizarine more readily," but the product could not be distinguished because it had "the same properties as vegetable alizarine." 111 U.S. at 300. Similarly, in *The Wood*

Paper Patent case, 90 U.S. 566 (1874), a new source of paper pulp that involved chemical and mechanical treatment made it "ready for washing and bleaching by a single operation," *id.* at 568, but "[i]t is with the finished article that the comparison must be made," and the absence of a "substantial difference" from the prior art necessarily rendered the patent "void for want of novelty." *Id.* at 596.

Therefore, this Court should reinstate the jury's verdict of anticipation.

II. The Fiers Patent Does Not Enable or Provide Written Description of the Full Scope of the Claims.

A separate and independent ground for reversal is that the Fiers Patent fails to satisfy the requirements of 35 U.S.C. § 112 as to the full scope of its astonishingly broad claims.

The enablement requirement in 35 U.S.C. § 112 enforces the bargain that underpins the patent system: In exchange for the limited monopoly a patent provides, it requires the inventor to teach the person of ordinary skill ("POSA") how to make and use the full scope of the claimed invention without undue experimentation. *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1352-53 (Fed. Cir. 2010) (en banc); *Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). Similarly, under Section 112's written de-

scription requirement, the "full scope" of the claim must be adequately described. *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014).

The Fiers Patent does not meet these requirements. As Appellants discuss in their opening brief, the patent claims the use of polypeptides made in a vast number of non-human hosts—polypeptides (and thus their use) that the patent does not enable or describe. That argument clearly is correct. Time and again, this Court has held that claims directed to recombinant expression in narrower categories of host cells than the Fiers Patent claims were not enabled even at later points in time. *In re Vaeck*, 947 F.2d 488, 495-96 (Fed. Cir. 1991) ("[H]eterologous gene expression in cyanobacteria [was] 'unpredictable'" as of 1987); *In re Goodman*, 11 F.3d 1046, 1052 (Fed. Cir. 2010) (claims to recombinant polypeptide expression in all plant cells were not enabled, where "[e]ach of the [recombinant expression] methods for monocot plants was fraught with unpredictability" as of 1985); *Adang v. Fischhoff*, 286 F.3d 1346, 1358 (Fed. Cir. 2002) (claims to recombinant expression in plant cells not enabled where art was "substantially unpredictable" as of 1986).

But claim 1 of the Fiers Patent is far too broad in another respect, which Appellants had no reason to address (at trial or on appeal) given that they also

were accused of infringing claim 2. Claim 1 encompasses not only the use of IFN-β itself—the polypeptide that Dr. Fiers was attempting to make—but of an unfathomably enormous genus of other polypeptides that Dr. Fiers did not invent, did not describe, and did not enable. Because these additional Section 112 infirmities are intertwined with those raised by Appellants, Bayer brings them to the Court's attention here.

This Court repeatedly has invalidated patents that, like the Fiers Patent, impermissibly "assert coverage of yet-unidentified ways of achieving a desired result" and "attempt to preempt the future before it has arrived." *GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 731 (Fed. Cir. 2014) (quoting *Fiers*, 984 F.2d at 1171). As the Supreme Court put it more than a hundred years ago, an applicant "can lawfully claim only what he has invented and described, and if he claims more his patent is void." *O'Reilly v. Morse*, 56 U.S. 62, 121 (1853). The district court erred as a matter of law in failing to apply these settled principles in this case, and further erred in articulating jury instructions that—if allowed to stand uncorrected—may also lead to error in any future trial against Bayer, in which the additional overbreadth of claim 1 would be at issue.

A. The District Court's Jury Instructions Were Legally Erroneous.

The district court erred by instructing the jury, over Appellants' objection, that "it is the method of treatment that must be described [and enabled], not the proteins to be used or the way they are made." Appx47670, Appx47672. In a series of unambiguous decisions, this Court has repeatedly required patentees to enable and describe the full scope of compositions used in method claims. "Regardless [of] whether a compound is claimed per se or a method is claimed that entails the use of the compound," the patent must "provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds," because the distinction between claims to a genus of compounds and a method of administering those compounds "is a semantic distinction without a difference." *Univ. of Rochester v. G.D. Searle*, 358 F.3d 916, 926, 929 (Fed. Cir. 2004).

Chief among the governing precedents is *Ariad*. Like this case, *Ariad* involved a method claim. The patent failed to describe the universe of possible compositions used in the claim, but the patentee argued that there was no written description problem because the claim was to a novel method. *Ariad*, 598 F.3d at 1354-55. The en banc Court disagreed, holding that the patent

"must adequately describe the claimed methods . . . *including adequate description of the molecules . . . necessary to perform the methods*." *Id.* at 1355 (emphasis added). The handful of example compounds the patent described could not "bear the weight of the vast scope of these generic claims." *Id.* at 1358. Under *Ariad*, to satisfy the written description requirement, the specification must either describe "a representative number of species falling within the scope of the genus," or identify "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," so as to distinguish the claimed species from unclaimed species. *Ariad*, 598 F.3d at 1350.

The district court refused to apply this controlling precedent. It based its jury instructions on an erroneous legal conclusion it had first reached when it confronted the mutein and non-human host issues at the summary judgment stage. At that stage, the district court incorrectly concluded that "it is not the genus of expression systems that must be enabled and described, it is the method of treatment that must be enabled and described." Appx46450. In concluding that a claim to a method of using a genus need not describe and enable the full scope of that genus, the district court relied on *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 2016 WL 6138124 (E.D. Tex. Oct. 21,

2016).[5] Appx46449-46450. But *UroPep* does not support the district court's interpretation of the law.

The *UroPep* court's reasoning did not turn on the fact that the claim was directed to the use of a genus rather than the genus itself; it focused on the fact that the claim was to a *novel use* of a known class of compounds. *UroPep*, 2016 WL 6138124, at *15-16.[6] This is consistent with this Court's teaching that "the *novel aspect* of an invention must be enabled," *Auto Techs. Int'l, Inc. v. BMW of N. Am., Inc.*, 501 F.3d 1274, 1283 (Fed. Cir. 2007) (emphasis added), and its recent reiteration that the Court has "generally eschewed judicial exceptions to the written description requirement based on the subject matter of the claims," *Amgen, Inc. v. Sanofi*, 872 F.3d 1367, 1379 (Fed. Cir. 2017).

[5] *Aff'd*, 739 F. App'x 643 (Fed. Cir. Oct. 10, 2018).

[6] In its brief on appeal in this Court, UroPep made clear that "[t]he district court's analysis did not turn on whether the patent claimed a method [of use], a compound, or a combination. Instead, the district court distinguished between claims where the *novel aspect* of the invention was a new chemical genus, versus claims where the novelty was a new use for a known class of compounds." No. 17-2603, D.I. 24, at 35 (emphasis added); *see also id.* at 25 ("[The novelty in this case is the method of treatment, not the PDE5 inhibitors").

Unlike the patent at issue in *UroPep*, the allegedly novel aspect of the Fiers Patent was *not* the method of treatment. Dr. Fiers never treated anyone, and the patent specification contains not a word about any novel treatment regimens or approaches. Biogen and its expert witnesses readily admitted that the Fiers Patent added nothing to the prior-art methods of using native IFN-β to treat the same conditions listed in the claims. *See* Appx81049 (175:15-22) ("Q: . . . all of that information in the '755 Patent about what you can do with interferon-beta, what diseases you can treat, how you treat it, what the results might be, how much you have to use, when you should give it, that was all known as to native interferon-beta at the time. Correct? And that's what's contained in that background section? A: Correct."); Appx81050 (176:18-22) ("Q: And so it's fair to say, isn't it, that there's no new information about treatment in the '755 Patent that wasn't already in the prior art from the 1970s pertaining to the use of native interferon-beta. We agree? A: We agree."). Indeed, when the patent examiner rejected the Fiers application as obvious over prior-art references disclosing treatment with native IFN-β, Biogen's response was not to assert any novel method of treatment, but rather to argue that "[b]ecause [Fiers's] claimed *recombinant polypeptides are novel* and non-obvious their use in a method for treating various diseases by *prior*

art methods must also be novel and non-obvious." Appx47849 (emphasis added).

Moreover, the district court's instructions in this case differed fundamentally from those given by the *UroPep* court. Even though that case involved a claim to a method of use, the court (Bryson, J., sitting by designation) instructed the jury, based on *Ariad*, that to satisfy the written description requirement, the patent must "include[] a sufficient number of representative compounds or a common structural feature so that a person of ordinary skill in the art would understand, from reading the patent, that the inventor invented the full scope of the claimed method." *UroPep*, 2:15-cv-01202-WCB (E.D. Tex. Apr. 25, 2017), D.I. 346, at 1427. Thus, far from concluding that the requirements for describing the full scope of a genus do not apply to a method claim, the *UroPep* court instructed the jury that those requirements *do* apply.[7] The district court in this case erroneously told the jury exactly the opposite—

[7] In its brief in this Court, UroPep made clear that it did not consider its claims to be exempt from *Ariad*'s requirements but rather that "UroPep's patent meets both standards set forth in *Ariad*." No. 17-2603, D.I. 24, at 15. As to enablement, too, UroPep conceded that its patent was required to enable the full scope of the genus, but it argued that it did so in light of "the maturity and predictability of the relevant field." *Id.* at 30. That rationale does not apply here, because recombinant technology was in its infancy in 1980.

that "the proteins to be used [and] the way they are made" need not be described and enabled.[8] Appx47670, Appx47672.

B. This Court Should Consider the Patent's Failure To Adequately Describe the Genus of Muteins in Framing the Correct Legal Standard and Jury Instructions, if Any Further Proceedings Are Necessary.

During summary judgment proceedings, Bayer argued to the district court that claim 1 of the Fiers Patent is invalid under Section 112 because the patent does not adequately describe the vast number of polypeptides used in the claimed method. Although this issue goes beyond the arguments raised by Appellants, it provides important background that this Court should consider if the Fiers Patent survives for further proceedings in the district court. Bayer addresses this issue here because of its potential impact on Biogen's separate case against Bayer.

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[8] Ultimately the jury in *UroPep* found that the challenger did not prove that the patent in that case was invalid for lack of enablement or written description. In then denying the defendant's motion for judgment as a matter of law, the court emphasized the evidence that hundreds of members of the genus were known as of the priority date and the field of the invention was "mature." 2:15-cv-1212-WCB (E.D. Tex. Nov. 3, 2017), D.I. 403, at 15-16. The opposite is true here. Moreover, in the summary judgment opinion cited by the district court here, the *UroPep* court recognized that a very different case would be presented if the patent had "disclosed very little information" or "provided no examples" of the members of the genus. 2016 WL 6138124, at *16. That is the case with the Fiers Patent.

The plain language of claim 1 encompasses using *any* polypeptide—regardless of its structure—so long as it (1) is encoded by DNA meeting the hybridization (or degeneracy) limitations and (2) exhibits antiviral activity. These limitations lead to an extraordinarily broad scope. As Biogen's own experts explained, because it is enough for only a *portion* of two DNA sequences to correspond for the molecules to hybridize, a mutein of IFN-β (which has 166 amino acids) may have "a stretch of 100, any hundred," Appx13879 (610:8-11), amino acids in common with interferon-beta, while "the other 66 amino acids *can be anything.*" Appx13879 (609:22-610:11) (emphasis added). Thus, the hybridization requirement encompasses a number of mutein polypeptides *many times larger than 19 to the 66th*—a 2 with 84 zeroes after it.[9]

Despite this enormous scope, the specification fails to disclose a single mutein within the scope of claim 1, discloses only the process of making one polypeptide (IFN-β) in two strains of *E. coli*, and mentions having made such polypeptides in unspecified "monkey cells"—added after the priority date—without discussing any of the details of that work. This narrow disclosure of a

[9] For an explanation of the calculation underlying this assertion, see Appx13879 (610:15-611:8).

single polypeptide, which is not even a mutein, is not a "representative number" of the trillions of muteins that are within the scope of the claims. *See Boston Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1357-58 (Fed. Cir. 2011) (holding that one disclosed compound was not representative of claimed genus of analogs); *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115 (Fed. Cir. 2008) (disclosure of single bacterial gene was not representative of generic claim). The patent's limited disclosure does not show with reasonable clarity that Dr. Fiers "actually invented" methods of treatment using this vast array of recombinant polypeptides. *Ariad*, 598 F.3d at 1351.

Biogen's claim 1 also is doomed by the requirement that the claimed polypeptides must have antiviral activity. The Fiers Patent fails to disclose—and the POSA could not know—which of the trillions of muteins that hybridize actually exhibit antiviral activity and thus could be used to treat viral conditions. Indeed, there is not a single representative example of a mutein that hybridizes and exhibits antiviral activity. Nor does the patent disclose structural features those polypeptides share, and what features they do not share, with inactive polypeptides.

Biogen's own experts admitted in their depositions that "there was no known correlation, as of June 1980, between the structure" or "sequence" of

"interferon-beta muteins and their activity in an anti-viral assay." Appx13880 (613:18-25); *see also* Appx13968 (74:7-75:11). Dr. Green testified clearly: the antiviral activity limitation "does not convey to a person of ordinary skill what structures the recombinant polypeptides have." Appx13882 (622:12-16). He also testified that "as of 1980 and probably . . . even as of today" there "was no known relationship between the structure of the recombinant polypeptides and the function of having antiviral activity." Appx13882 (622:17-623:22). Rather, he agreed that "nothing at all was known about interferon-beta muteins" as of June 1980. Appx13880 (615:14-24). And, he testified, the Fiers Patent "provides no guidance" as to "which of those muteins would be active and which of them would not be active." Appx13882 (622:13-20). Dr. Garcia agreed that, given the lack of a known structure-function relationship, the POSA would have to assay each mutein individually for activity to determine whether it fell within the claim. Appx13968 (74:7-75:11).[10]

Moreover, the Fiers Patent does not describe or enable the full scope of claim 1 even under the district court's incorrect post-verdict definition, which

[10] These depositions are not in the trial record, but Bayer does not ask this Court to consider them as a basis for its decision in this case. Rather, Bayer cites them only to inform the Court concerning a separate case on which the Court's decision may have an impact.

emphasized that "for a polypeptide to display biological activity, it must be folded into its appropriate three-dimensional structure." Appx23. The Fiers Patent fails to describe how to differentiate muteins that would fold properly from those that would not. As Biogen's expert, Dr. Garcia, testified at trial, "there's an almost infinite number of conf[o]rmations and folding pathways" that a polypeptide of IFN-β's size can assume, yet "it has to find the perfect folding pathway" to be biologically active. Appx80476-80477 (62:20-63:5). And as Dr. Garcia testified in his deposition, if "a folding problem in *E. coli*" prevented biological activity, "there could always be another expression system that might fold the thing [i.e., a polypeptide with the same amino acid sequence] correctly and have activity." Appx13969 (79:13-24). But it would be impossible to know which permutation would work without testing each polypeptide, as made by each potential host, Appx13969 (79:13-80:21)—thus further multiplying the trillions of possible muteins that must be tested by the millions of potential hosts.

Under the plain language of the jury instructions that the district court erroneously applied against Appellants, there apparently was no need for Dr. Fiers to describe or enable the use of the myriad unidentified polypeptides within this vast universe that may have antiviral activity. The court expressly

stated that "the proteins to be used" need not be described or enabled. While this infirmity in claim 1 is not directly at issue in this appeal, it further illustrates the Section 112 problems of the Fiers Patent and the consequences of the district court's errors.

CONCLUSION

The judgment below should be reversed.

Respectfully submitted,

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APRIL 15, 2019

CERTIFICATE OF SERVICE

I, Bruce R. Genderson, hereby certify that on April 15, 2019, I caused the foregoing document to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification to the registered attorneys of record that the document has been filed and is available for viewing and downloading.

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APRIL 15, 2019

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Federal Circuit Rule 32(a) and Federal Rule of Appellate Procedure 29(a)(5). The brief contains 6287 words, excluding the parts of the brief exempted by Federal Rule of Appellate Procedure 32(f).

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