**No. 2020-1933**

# UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BIOGEN INTERNATIONAL GMBH, BIOGEN MA INC.,

*Plaintiffs-Appellants*,

*v.*

MYLAN PHARMACEUTICALS INC.,

*Defendant-Appellee.*

On Appeal from the United States District Court for the Northern District of West Virginia, No. 1:17-cv-00116-IMK-JPM, Judge Irene M. Keeley

## PLAINTIFFS-APPELLANTS BIOGEN INTERNATIONAL GMBH AND BIOGEN MA INC.'S COMBINED PETITION FOR PANEL REHEARING AND REHEARING EN BANC

THOMAS G. SAUNDERS
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue NW
Washington, DC 20006
(202) 663-6000

JAMES B. MONROE
PAUL W. BROWNING
J. MICHAEL JAKES
JASON L. ROMRELL
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, LLP
901 New York Avenue, NW
Washington, DC 20001-4413
(202) 408-4000

WILLIAM F. LEE
LISA J. PIROZZOLO
ANNALEIGH E. CURTIS
MADELEINE C. LAUPHEIMER
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

SCOTT G. GREENE
WILMER CUTLER PICKERING
HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

December 30, 2021

# CERTIFICATE OF INTEREST

Counsel for Plaintiffs-Appellants Biogen International GmbH and Biogen MA Inc. certifies the following:

**1. Represented Entities**. Fed. Cir. R. 47.4(a)(1). Provide the full names of all entities represented by undersigned counsel in this case.

Biogen International GmbH and Biogen MA Inc.

**2. Real Party in Interest**. Fed. Cir. R. 47.4(a)(2). Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities.

None.

**3. Parent Corporations and Stockholders**. Fed. Cir. R. 47.4(a)(3). Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities.

Biogen International GmbH and Biogen MA Inc. are owned directly, or indirectly, by Biogen Inc.

**4. Legal Representatives**. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

SCHRADER COMPANION DUFF & LAW, PLLC: James F. Companion, Frank X. Duff, Sandra K. Law, Travis L. Zeik

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, LLP: Aaron G. Clay, Lauren J. Dowty, Mark J. Feldstein, Li Feng, Eric J. Fues, Laura P. Masurovsky, Megan L. Meyers, John E. Nappi, Andrew E. Renison, Jeanette M. Roorda, Sanya Sukduang

**5. Related Cases**. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

*Mylan Pharmaceuticals Inc. v. Biogen MA Inc.*, No. 2020-1673 (Fed. Cir.)

*Biogen International GmbH, et al. v. Amneal Pharmaceuticals LLC, et al.*, Nos. 2021-1078, -1084, -1086, -1087, -1088, -1090, -1091, -1092, -1093, -1094, -1095, -1096, -1097, -1098 (Fed. Cir.)

*Biogen MA Inc. v. Sun Pharmaceutical Industries, et al.*, No. 2021-1441 (Fed. Cir.)

*Biogen MA Inc. v. Windlas Healthcare Pvt. Ltd.*, No. 1:17-cv-00849 (D. Del.)

*Biogen International GmbH, et al. v. Torrent Pharmaceuticals Ltd., et al.*, No. 1:17-cv-00854 (D. Del.)

*Biogen International GmbH, et al. v. Macleods Pharmaceuticals, Ltd., et al.*, No. 1:17-cv-00857 (D. Del.)

**6. Organizational Victims and Bankruptcy Cases**. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

None.

Dated: December 30, 2021

/s/ William F. Lee

WILLIAM F. LEE
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

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## STATEMENT OF COUNSEL

Based on my professional judgment, I believe the panel decision is contrary to the following precedents of the Supreme Court and this Court: *Schriber-Schroth Co. v. Cleveland Trust Co., Chrysler Corp*., 305 U.S. 47 (1938); *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co*., 598 F.3d 1336 (Fed. Cir. 2010) (en banc); *Alcon Research Ltd. v. Barr Laboratories, Inc.*, 745 F.3d 1180 (Fed. Cir. 2014).

Based on my professional judgment, I also believe this appeal requires an answer to the following precedent-setting questions of exceptional importance:

1. Does 35 U.S.C. § 112's requirement to provide "a written description of the invention" require that the specification prove the invention's efficacy?

2. Does a specification that discloses multiple embodiments have to repeatedly describe and single out the claimed embodiment?

3. May a court of appeals defer to a district court's factfinding while declining to address multiple legal errors that skewed that factfinding?

/s/ William F. Lee
WILLIAM F. LEE

## POINTS OF FACT OR LAW OVERLOOKED OR MISAPPREHENDED BY THE COURT

The panel majority misapprehended *Schriber-Schroth*, *Ariad*, and *Alcon* and applied a heightened written description standard when it held that the disclosure of "from about 480 mg to about 720 mg per day" as an "effective" amount of DMF, Appx74(18:58-62), did not adequately describe the claimed dose of "480 mg per day." The decision required disclosure of actual reduction to practice, such as data proving clinical efficacy, rather than "a written description of the invention." Op. 17-18. It also strayed from precedent when it faulted Biogen because the claimed dose was "not listed as an independent therapeutically efficacious dose" and was "listed only once." Op. 16-17. The panel majority also incorrectly deferred to the district court's factual findings while expressly declining to consider errors of law underlying those findings. Op. 19-20.

## INTRODUCTION

Since *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, 598 F.3d 1336 (2010) (en banc), some courts—including the district court in this case—have struggled with the concept of showing "possession" of a claimed invention. Over a dissent by Judge O'Malley, the panel majority added to that confusion and broke with prior precedent to create a new, more stringent written description requirement.

Biogen's patent claims methods of treating multiple sclerosis ("MS") by orally administering a therapeutically effective amount of dimethyl fumarate ("DMF"), wherein the therapeutically effective amount is about 480 mg/day ("DMF480"). The district court found that a Biogen scientist had conceived the claimed invention. Appx5-6. Biogen's specification linked all elements of the claimed invention, and expressly stated that "an effective dose of DMF or MM[F] to be administered to a subject orally can be … from about 480 mg to about 720 mg per day," Appx74(18:58-62). The panel majority nonetheless held that this disclosure did not show possession of the claimed DMF480 dose, noting that Biogen had not yet conducted its Phase III clinical trials, Op. 17, and the "DMF480 dose is listed only once," Op. 16-17.

The panel majority's decision departs from precedent and 35 U.S.C. § 112's plain text requiring "a written description of the invention," and instead requires

that the specification itself *prove* the described effect. The panel majority thus incorrectly treated the written description requirement as if it mandated actual reduction to practice.

Moreover, in faulting Biogen for describing the claimed dose "only once," the panel majority further misinterpreted the written description requirement. There is no requirement that a specification repeat or single out a claimed embodiment. The specification described DMF480 as the lowest endpoint of the narrowest range of disclosed effective doses. As the dissent asked, even if this Court's "blaze marks" test applied, "How much brighter need a disclosure blaze?" Dissent 11. The panel majority's holding that such a disclosure is insufficient conflicts with precedent and will have far-reaching consequences for myriad patents that disclose multiple embodiments, particularly patents that follow the common convention of disclosing nested and progressively narrowing ranges.

Finally, the panel majority compounded these errors by deferring to the district court's factfinding while refusing to review the legal errors underlying it. For example, there was "no dispute" that "the district court erred in finding that Biogen was judicially estopped" from arguing that the specification did not need to disclose the level of clinical efficacy the DMF480 dose demonstrated in Phase III clinical trials. Dissent 1. The district court also disregarded the specification's definition of the claim term "therapeutically effective amount." Furthermore, the

district court misinterpreted precedent to "find that the '514 patent does not demonstrate possession because it lacks clinical efficacy data," Dissent 6, and to "conflate concepts of obviousness and written description" by "overlay[ing] a POSA's reasonable expectation of success from the obviousness context onto the written description inquiry," Dissent 6-7.

These and other legal errors needed to be addressed *before* any deference was given to the district court's factfinding on written description. But the panel majority approached the task backwards, by erroneously concluding that its affirmance of the district court's factfinding under a deferential standard of review rendered "superfluous" Biogen's challenges to the legal errors that drove that factfinding. Op. 20.

The Court should grant panel rehearing or rehearing en banc to restore the proper interpretation of the written description requirement.

## BACKGROUND

### I. BIOGEN'S DEVELOPMENT OF TECFIDERA®

In 2003, based on confidential data and consideration of DMF's pharmacology, Biogen scientist Dr. Gilmore O'Neill conceived of treating MS with an oral dose of 480 mg/day of DMF. Appx6; Appx1586-1587; Appx1612-1613; Appx2133-2134. At the time, the only FDA-approved drugs for treating MS were administered by injection.

Biogen did not immediately put Dr. O'Neill's invention into clinical trials. Instead, Biogen's Phase II study tested the clinical efficacy of the lower and higher DMF doses of 120, 360, and 720 mg/day. Appx2184; Appx2188. The results showed that 720 mg/day ("DMF720") effectively treated MS based on certain MRI endpoints, but that the 120 and 360 mg/day doses had no statistically significant clinical effect. Appx2188-2191; Appx1708; Appx2052-2059(¶¶6-10).

Biogen's Phase III trials included the 480 mg/day dose Dr. O'Neill had wanted to test, as well as the DMF720 dose tested in Phase II. The DMF480 dose not only met all MRI endpoints and clinical endpoints "with a high level of statistical significance," but unexpectedly performed similarly on each clinical endpoint to the higher DMF720 dose, which had itself outperformed its own Phase II results. Appx2059-2069(¶¶11-12, 15) (emphasis omitted). In 2013, the FDA approved administration of a 480 mg/day dose of DMF, which Biogen markets as Tecfidera®.

## II. THE '514 PATENT

U.S. Patent No. 8,399,514 ("the '514 patent") claims priority to a provisional application Biogen filed in February 2007, between its Phase II and

Phase III studies. Appx52; Appx3290-3291. The priority application disclosed both methods of screening compounds and methods of treatment. Appx3295.[1]

MS is disclosed throughout the specification. Appx66(1:12-52); Appx67(3:10-14); Appx69(7:13-15); Appx73(16:21-26). Method 4 discloses administration of a "therapeutically effective amount" of DMF, Appx67(4:29-32), and describes administering the compound in an amount "sufficient to slow or prevent demyelination, axonal loss, and/or neuronal death," Appx67(4:33-38). The specification's definition of "therapeutically effective amount" highlights the same outcomes, Appx68(5:52-59), which involve characteristics the parties agreed would be recognized as hallmarks of MS. Appx1461-1462; Appx1501-1502.

Column 18 addresses the dose to be used in Method 4. Column 18 discloses a few increasingly narrow dosing ranges and, in the narrowest range, states that "an effective dose of DMF … to be administered to a subject orally can be … from about 480 mg to about 720 mg per day." Appx74(18:58-62).

The specification thus describes claim 1 of the '514 patent, which states:

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[1] The application was originally titled "NRF2 Screening Assays and Related Methods and Compositions," and Dr. Matvey Lukashev was named as the inventor based on his contributions relating to the Nrf2 pathway. Appx3290-3291; Appx3337. In June 2011, Biogen amended the title to "Treatment for Multiple Sclerosis" and listed Dr. O'Neill as a named inventor to reflect the prosecution of claims to specific methods of treatment disclosed in the specification that were based on his inventive contribution. Appx3437-3439.

> A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject in need thereof a pharmaceutical composition consisting essentially of (a) a therapeutically effective amount of dimethyl fumarate [DMF], monomethyl fumarate, or a combination thereof, and (b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof is about 480 mg per day.

Appx79.

## III. THE DISTRICT COURT'S DECISION

After receiving a Hatch-Waxman notice, Biogen sued Mylan in the Northern District of West Virginia. Appx6001-6002. Mylan stipulated to infringement but asserted invalidity. Appx6154-6157. At trial, Mylan's expert argued that the claims were obvious and testified that a skilled artisan "would have a reasonable expectation of success in treating multiple sclerosis patients with 480 milligrams a day of dimethyl fumarate." Appx1116-1117. But in the middle of trial, the Patent Trial and Appeal Board ("PTAB") issued a final written decision finding that the claims were not obvious. *Mylan Pharms. Inc. v. Biogen MA Inc*., IPR2018-01403, Paper No. 98 (P.T.A.B. Feb. 5, 2020). Mylan, estopped from arguing obviousness, then shifted to arguing lack of written description, claiming that a skilled artisan would not understand that Biogen possessed the DMF480 dose.

The district court held that the claims of the '514 patent were invalid for lack of written description. Appx3. But the decision never considered the definition of "therapeutically effective amount"—a claim term defined in, and used throughout,

the specification. Conflating the concepts of obviousness and written description, the district court also concluded that Biogen was judicially estopped from distinguishing the therapeutic efficacy required by the claims from the unexpected clinical efficacy of DMF480 demonstrated in Phase III trials and relied on by the PTAB in finding nonobviousness. Appx24 n.15.

Relatedly, the district court criticized the patent for failing to include "examples discussing efficacy data"; "graphs or data regarding proportion of relapses" and other metrics; or "Phase I data." Appx41-42. Again, conflating the concepts of obviousness and written description, the district court found these omissions "particularly telling" in its written description analysis "because a POSA would not have expected a 480mg/day dose of DMF (BID) to be efficacious in 2007" and "the efficacy of the 480mg/day dose of DMF (BID) was 'unexpected' four years later." Appx41.

In sum, the district court found that Dr. O'Neill had conceived of the invention in 2003 and had a "strong belief that a 480mg/day dose of DMF (BID) would effectively treat MS," Appx39; Appx5-6; Appx1612-1613, but the court found a lack of written description because Dr. O'Neill and Biogen allegedly "did not know that to be true" until Biogen's Phase III study results, Appx39.

## IV. THE PANEL MAJORITY'S DECISION

On November 30, 2021, a divided panel of this Court affirmed. Over a dissent by Judge O'Malley, the panel majority held that Biogen had not shown possession of the DMF480 dose despite it being expressly disclosed in Column 18 of the specification as an endpoint of the narrowest range of effective doses. Op. 22.

In her dissent, Judge O'Malley observed that the district court "conflate[d] concepts of obviousness and written description" and misinterpreted Federal Circuit precedent when it found that Biogen's patent "does not demonstrate possession because it lacks clinical efficacy data." Dissent 6. She also noted that the district court's "erroneous judicial estoppel ruling" was a "threshold error" that "impacted the district court's entire written description analysis." Dissent 1, 3. Judge O'Malley further explained that the Federal Circuit's "'blaze marks' precedent is not applicable," but even if that framework applied, "Column 18 provides a sufficient 'blaze mark' by explicitly mentioning the claimed DMF480 dose." Dissent 11.

# ARGUMENT

## I. THE PANEL MAJORITY'S DECISION APPLIES A HEIGHTENED WRITTEN DESCRIPTION REQUIREMENT

Section 112 requires that a patent's specification contain "a written description of the invention"—no more and no less. 35 U.S.C. § 112. The panel

majority's decision transforms that straightforward requirement into a heightened standard that conflicts with the statute and precedent.

### A. The Panel Majority Incorrectly Interpreted 35 U.S.C. § 112 To Require That Biogen *Prove* The Efficacy Of Its Claimed Method Rather Than *Describe* The Claimed Invention

The written description requirement helps "inform the public during the life of the patent of the limits of the monopoly asserted." *Schriber-Schroth Co. v. Cleveland Trust Co., Chrysler Corp*., 305 U.S. 47, 57 (1938) (quotation marks omitted). To satisfy the requirement, the specification must "allow one skilled in the art to visualize or recognize the identity" of the claimed subject matter. *Alcon Research Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190 (Fed. Cir. 2014) (quotation marks and alteration omitted). Written description does not require proof that an invention works, and "there is no requirement that the disclosure contain 'either examples or an actual reduction to practice.'" *Id*.

The panel majority deviated from this settled law to find inadequate written description despite the specification's description of DMF480, Appx74(18:58-62), and the district court's express finding that the inventor had conceived the claimed invention before the earliest priority date, Appx5-6. For example, citing *Ariad*, the panel majority stated that "[r]egardless of whether O'Neill had in fact hypothesized or even conceived the idea" of DMF480, "the law is clear that a patent cannot be awarded for mere theoretical research without more" because the "written-

description requirement limits patent protection only to individuals who perform the difficult work of producing a complete and final invention." Op. 18.[2]

This conclusion fundamentally misunderstands *Ariad*. The patent at issue in *Ariad* claimed a functional result without adequately describing what compounds would achieve that result. 598 F.3d at 1355-1357. By contrast, Biogen's patent described and linked all elements of the claimed invention, including the "effective" DMF480 dose. Holding that the description in *Ariad* was insufficient because it did not identify the compounds being claimed is fundamentally different from holding that Biogen's disclosure of the claimed invention was insufficient because Biogen had not completed its clinical trials. Under the panel majority's approach, it was not sufficient that Dr. O'Neill conceived of the invention and constructively reduced it to practice by describing it in a patent application. Rather, Biogen's specification would have had to include clinical trial results to satisfy the heightened written description requirement applied by the panel majority.

[2] The panel majority cited irrelevant testimony of Dr. Lukashev, the other named inventor on the '514 patent, to the effect that *his* work had not focused on the clinical dosing of DMF. Op. 16. But the district court found that Dr. O'Neill conceived of the asserted claims, Appx6, and Dr. Lukashev was *not* a skilled artisan for purposes of those claims, Appx34 n.18.

The panel majority exacerbated its error by framing the question before it as whether—"before the Phase III study even commenced—a skilled artisan could deduce simply from reading the specification that DMF480 would be a therapeutically effective treatment for MS." Op. 17. But where a patent expressly describes a dose as effective, a skilled artisan is not required to "deduce" anything. The '514 patent's specification expressly stated that "an effective dose of DMF … to be administered to a subject orally can be … from about 480 mg to about 720 mg per day." Appx74(18:58-62). As this Court has previously explained, "written description is about whether the skilled reader of the patent disclosure can recognize that what was claimed corresponds to what was described; it is not about whether the patentee has proven to the skilled reader that the invention works, or how to make it work." *Alcon*, 745 F.3d at 1191.

The panel majority's approach mirrored the error of the district court, which as the dissent explains, erroneously found "that the '514 patent does not demonstrate possession because it lacks clinical efficacy data," Dissent 6. The panel majority's heightened written description standard will effectively require actual reduction to practice, such as completed clinical trials, before a patent application can be filed. This would be a significant change in the written description requirement and would impose a standard not required by the statute or precedent.

The heightened standard would make it particularly difficult, if not impossible, to patent groundbreaking treatment claims. In practice, most clinical study details, including dose information, must be publicly disclosed to facilitate recruitment and begin the clinical trial. But the panel majority's heightened standard creates a Catch-22: a patent application must be filed before clinical trials to avoid the risk of invalidation for anticipation or obviousness, but then is at risk of invalidation for lack of written description for not including data from those same clinical trials.

### B. The Panel Majority Incorrectly Implied That The Specification Must Repeatedly Describe And Single Out The Claimed Dose

The panel majority again heightened the written description standard when it criticized Biogen's specification for mentioning DMF480 only "once" at "the end of one range among a series of ranges." Op. 16. The panel majority seemed to imply that only DMF720 was sufficiently described, because it was "referenced independently as one dose and was known to be effective as of the … priority date." *Id*.

The panel majority's approach to the disclosure of multiple embodiments is contrary to precedent. No decision holds that Section 112 requires repetition of a claim element. Moreover, "[t]he disclosure of a dose outside of the claimed range does not compel a finding that the asserted claims lack adequate written description." *Vanda Pharms. Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117,

1137 (Fed. Cir. 2018) (holding that disclosure of "reduced dosage of 18, 12, or 6 mg per day" supported claims to reduced dosage of "12 mg/day or less"). Similarly, "the listing of several inoperative species" does not give rise to a failure of written description "when the species claimed is operative and performs" as described. *Snitzer v. Etzel*, 465 F.2d 899, 902 (C.C.P.A. 1972).

Here, the specification listed only four, increasingly narrow dose ranges. The DMF480 dose was specifically named, along with the other dose tested in Biogen's Phase III trials (DMF720), as an endpoint of the narrowest range described in the specification as "effective." As Judge O'Malley noted, it would have been one thing to require blaze marks if the patent had disclosed a 100-720 mg range and then "expected a POSA to figure out that a 480 mg per day dose was therapeutically effective." Dissent 11. But "the range provided in Column 18 particularly points out the claimed DMF480 dose," prompting Judge O'Malley to ask: "How much brighter need a disclosure blaze?" Dissent 11; *see also Singh v. Brake*, 317 F.3d 1334, 1344 (Fed. Cir. 2003) (disclosure that "n is 0 or 1 to 4" was "a clear 'blaze mark' providing *in ipsis verbis* support for 'n = 0'").

The panel majority's insistence on further repetition or singling out, if allowed to stand, would have far-reaching consequences. It would mean that a patent application disclosing multiple embodiments could claim only the embodiment on which it places special emphasis or that it describes as most

preferred.[3] The consequences would impact many fields of technology but would fall particularly hard on patents in the biopharmaceutical industry and other industries where disclosing nested and progressively narrowing ranges, as Biogen did, is common.

## II. THE PANEL MAJORITY INCORRECTLY DECLINED TO ADDRESS MULTIPLE LEGAL ERRORS BASED ON DEFERENCE TO FACTFINDING SKEWED BY THOSE LEGAL ERRORS

Biogen's appeal focused primarily on a series of legal challenges to the analytical framework that the district court used to reach its finding regarding written description. However, the panel majority declined to consider these legal errors, concluding that its deference to the district court's factual finding on written description "render[ed] all these [legal] arguments superfluous." Op. 20. This was illogical and contrary to precedent. District court findings are not entitled to deference when they are based on misunderstandings of the law. *See Alcon*, 745 F.3d at 1190-1192 (reversing finding of lack of written description because the district court misinterpreted the written description requirement). The panel

[3] The district court made this mistake when it treated testimony from Biogen's expert that he did not know which dose "would be *most effective* for treating MS" as a "[t]elling[]" concession. Appx31 (emphasis added). But a dose need not be the most effective or most preferred to be described. *See ScriptPro LLC v. Innovation Assocs., Inc.*, 833 F.3d 1336, 1341 (Fed. Cir. 2016) ("[A] specification's focus on one particular embodiment or purpose cannot limit the described invention where that specification expressly contemplates other embodiments or purposes.").

majority therefore could not defer to those findings without any consideration of the legal framework applied in making them.

Here, the district court's legal errors had a significant impact on its written description finding. For example, the district court incorrectly held that Biogen was judicially estopped from pointing out what written description of the claims required. As Judge O'Malley noted, "[t]here is no dispute over whether the district court erred in finding that Biogen was judicially estopped from drawing a distinction between clinical and therapeutic effects: it did." Dissent 1. "[T]his threshold error impacted the district court's entire written description analysis." Dissent 1. Instead of examining whether the specification described the "therapeutically effective amount" required by the claims, the district court demanded proof of clinical efficacy. Dissent 2-4, 6.

The district court's erroneous judicial estoppel ruling also skewed its findings with respect to Biogen's expert, Dr. Wynn. What the district court perceived as a concession or discrediting inconsistency, Appx31, was, in reality, nonobviousness testimony in which Dr. Wynn, discussing the unexpected Phase III clinical results, said he would not have expected the DMF480 dose to be "clinically effective" in the way Biogen's trials demonstrated. Appx32-33; *see also* Appx1553-1554. The district court's judicial estoppel ruling and corresponding failure to consider the definition of "therapeutically effective

amount" in the patent led it to misunderstand this testimony and confuse the obviousness and written description inquiries.

The district court also imposed a heightened standard for written description. As Judge O'Malley explained, "after acknowledging that clinical data demonstrating effectiveness is not required to satisfy written description, the district court went on to find that the '514 patent does not demonstrate possession because it lacks clinical efficacy data." Dissent 6. This demand for clinical data arose from the district court's misinterpretation of *Nuvo Pharmaceuticals (Ireland) Designated Activity Co. v. Dr. Reddy's Laboratories Inc.*, 923 F.3d 1368 (Fed. Cir. 2019). Dissent 7-8. *Nuvo* analyzed written description in the unusual context of a specification that expressly taught away from the later-claimed invention, but the district court misread *Nuvo* to "overlay a POSA's reasonable expectation of success from the obviousness context onto the written description inquiry." Dissent 7. That misunderstanding confuses the "distinct question[s]" of "[w]hat a POSA would expect regarding clinical efficacy based on the prior art" and "whether a POSA would understand that the inventor possessed the *claimed* invention … based on the patent's written description." Dissent 8. The district court also misapplied and heightened the "blaze marks" test. Dissent 11.

Deferring to factfinding based on written description's classification as a question of fact, without squarely addressing the legal errors underlying that

factfinding, effectively removes meaningful appellate review when a district court's factfinding is influenced by a misunderstanding of the law.

## CONCLUSION

Biogen respectfully requests that the Court grant panel or en banc rehearing.

Respectfully submitted,

/s/ William F. Lee

WILLIAM F. LEE
LISA J. PIROZZOLO
ANNALEIGH E. CURTIS
MADELEINE C. LAUPHEIMER
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

SCOTT G. GREENE
WILMER CUTLER PICKERING
HALE AND DORR LLP
7 World Trade Center
250 Greenwich Street
New York, NY 10007
(212) 230-8800

*Attorneys for Plaintiffs-Appellants Biogen International GmbH and Biogen MA Inc.*

THOMAS G. SAUNDERS
WILMER CUTLER PICKERING
HALE AND DORR LLP
1875 Pennsylvania Avenue NW
Washington, DC 20006
(202) 663-6000

JAMES B. MONROE
PAUL W. BROWNING
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, LLP
901 New York Avenue, NW
Washington, DC 20001-4413
(202) 408-4000

December 30, 2021

# ADDENDUM

# United States Court of Appeals for the Federal Circuit

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**BIOGEN INTERNATIONAL GMBH, BIOGEN MA, INC.,**
*Plaintiffs-Appellants*

**v.**

**MYLAN PHARMACEUTICALS INC.,**
*Defendant-Appellee*

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2020-1933

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Appeal from the United States District Court for the Northern District of West Virginia in No. 1:17-cv-00116-IMK-JPM, Judge Irene M. Keeley.

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Decided: November 30, 2021

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WILLIAM F. LEE, Wilmer Cutler Pickering Hale and Dorr LLP, Boston, MA, argued for plaintiffs-appellants. Also represented by ANNALEIGH E. CURTIS, MADELEINE C. LAUPHEIMER, LISA JON PIROZZOLO; SCOTT G. GREENE, New York, NY; THOMAS SAUNDERS, Washington, DC; PAUL WILLIAM BROWNING, J. MICHAEL JAKES, JAMES B. MONROE, JASON LEE ROMRELL, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, Washington, DC.

DAVID LEE ANSTAETT, Perkins Coie, LLP, Madison, WI, argued for defendant-appellee. Also represented by ANDREW DUFRESNE, EMILY JANE GREB; DAN L. BAGATELL, Hanover, NH; SHANNON BLOODWORTH, NATHAN K. KELLEY, BRANDON MICHAEL WHITE, Washington, DC; MATTHEW GREINERT, Mylan, Canonsburg, PA.

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Before O'MALLEY, REYNA, and HUGHES, *Circuit Judges*.

Opinion for the court filed by *Circuit Judge* REYNA.

Dissenting opinion filed by *Circuit Judge* O'MALLEY.

REYNA, *Circuit Judge*.

This appeal from the United States District Court for the Northern District of West Virginia concerns a patent-infringement dispute between Biogen International GmbH, Biogen MA, Inc., and Mylan Pharmaceuticals, Inc. Biogen owns United States Patent 8,399,514 (the '514 Patent), which claims a method of treating multiple sclerosis with a drug called dimethyl fumarate. In 2017, Biogen filed a lawsuit against Mylan alleging patent infringement. Mylan counterclaimed for declaratory judgment that the patent was invalid and not infringed. Following a bench trial, the district court determined that the asserted claims of the '514 Patent were invalid for lack of written description. Biogen challenges the district court's decision on appeal.

For the reasons set forth in this opinion, we hold that the district court did not clearly err in determining that Mylan has established its burden of showing, by clear and convincing evidence, that the asserted '514 Patent claims are invalid for lack of written description under 35 U.S.C. § 112. Accordingly, we affirm the judgment of the district court.

## I. BACKGROUND

Under the Drug Price Competition and Patent Term Restoration Act of 1984 (the Hatch-Waxman Act), a manufacturer of a new generic drug that is bioequivalent[1] to a previously approved drug may seek approval from the US Food and Drug Administration (FDA) to market the generic product by filing an Abbreviated New Drug Application (ANDA). *See* Pub. L. No. 98-417, § 101, 98 Stat. 1585, 1585–86 (1984) (codified as amended at 21 U.S.C. § 355(j)(2)(A)). The statute requires the generic-drug manufacturer to submit a certification regarding the status of

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[1] For purposes of Hatch-Waxman litigation, a generic drug is considered bioequivalent to a brand-name drug if:

> (i) the rate and extent of absorption of the [generic] drug do not show a significant difference from the rate and extent of absorption of the listed [brand-name] drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or
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> (ii) the extent of absorption of the [generic] drug does not show a significant difference from the extent of absorption of the listed [brand-name] drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

21 U.S.C. § 355(j)(8)(B)(i)–(ii).

any patent that purportedly protects the brand-name drug, including information as to whether no such patent exists or the patent already expired, and if the patent has not expired the manufacturer must indicate the date on which the patent will expire. 21 U.S.C. § 355(j)(2)(A)(vii)(I)–(III).

If a patent that covers the brand-name drug has not expired, the generic-drug manufacturer may file what is known as a paragraph IV certification, attesting that the "patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted." *Id.* § 355(j)(2)(A)(vii)(IV). The manufacturer filing the ANDA and paragraph IV certification must promptly notify the owner of any patent subject to the certification. *Id.* § 355(j)(2)(B)(iii). And the FDA must approve the ANDA, unless the patent owner objects by filing an action for patent infringement against the generic-drug manufacturer within forty-five days of receiving notice of the paragraph IV certification. *Id.* § 355(j)(5)(B)(iii). If the patent owner brings the infringement suit under the Hatch-Waxman Act within the statutory period, the law triggers an automatic, thirty-month stay in the FDA-approval process of the generic drug, pending the outcome of the litigation. *See id.* § 355(j)(5)(B)(iii).

Mylan Pharmaceuticals, Inc. (Mylan) filed an ANDA seeking to manufacture, use, and market a generic dimethyl fumarate (DMF) product for the treatment of multiple sclerosis (MS) before the expiration date of the '514 Patent. J.A. 6001–02. On June 30, 2017, Biogen International GmbH and Biogen MA, Inc. (collectively Biogen) sued Mylan for patent infringement in the Northern District of West Virginia pursuant to the Hatch-Waxman Act. *Id.* In its original complaint, Biogen asserted six patents[2]

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[2] In addition to the '514 Patent, Biogen asserted US Patents 6,509,376; 7,320,999; 7,619,001; 7,803,840; and 8,759,393. J.A. 6002.

purportedly covering Tecfidera®, Biogen's trademarked DMF-capsule formulation for the treatment of patients suffering from relapsing-remitting forms of MS. *Id.* Only the '514 Patent is at issue in this appeal. *See* J.A. 2–3.

A. The '514 Patent

The '514 Patent claims priority to United States Provisional Application 60/888,921 (the '921 Application), which Biogen filed on February 8, 2007. U.S. Patent No. 8,399,514, at [60] (filed Feb. 13, 2012) (issued Mar. 19, 2013). As issued, the patent is entitled "Treatment for Multiple Sclerosis." '514 Patent, at [54].

MS is a disabling autoimmune disease that affects the central nervous system (CNS) and involves an abnormal inflammatory response, which leads to damage and the eventual destruction of the myelin sheath that surrounds neuronal axons—the nerve fibers that transmit electrical signals across CNS nerve cells. *See* '514 Patent col. 1 ll. 15–20. The myelin sheath, which comprises a mixture of proteins and lipids, is a substance that acts as a protective covering to insulate nerve fibers—much like the insulation material that surrounds and protects an electrical wire—and permits nerve cells to adequately conduct the electrical signals. *See* John S. O'Brien, *Stability of the Myelin Membrane*, 147 SCIENCE 1099, 1099 (1965); J.A. 4–5. MS-induced deterioration of the myelin sheath interferes with the proper transmission of such electrical signals across nerve cells and eventually contributes to neurodegeneration, death of neurons, and progressive neurological dysfunction in individuals suffering from the disease. *See* '514 Patent col. 1 ll. 17–20, 29–30; J.A. 4–5.

In its action alleging patent infringement against Mylan, Biogen asserted claims 1–4, 6, 8–13, 15, and 16 of the '514 Patent. J.A. 15–17. Claim 1 is representative and recites:

> A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject in need thereof a pharmaceutical composition consisting essentially of (a) a therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof, and (b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of dimethyl fumarate, monomethyl fumarate, or a combination thereof is about 480 [milligrams] per day [(mg/day)].

*Id.* col. 27 ll. 59–67. Relevant to this appeal is Biogen's use of DMF, a fumaric-acid ester compound, at a specific dose of 480 mg/day (DMF480) under the brand name Tecfidera® for the treatment of MS.

The '514 Patent specification largely tracks that of the original '921 Application, which Biogen entitled "Nrf2 Screening Assays and Related Methods and Compositions."[3] J.A. 3289–92. The specification casts a wide net for a myriad of neurological disorders, including neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease; demyelinating neurological diseases, such as various forms of MS and at least twenty-eight other disorders related to demyelination; polyneuritis; and mitochondrial disorders with demyelination. *See* '514 Patent col. 16 ll. 18–63. Although the specification does not focus exclusively on MS, it discusses MS-related background

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[3] On February 7, 2008, Biogen filed International Patent Application PCT/US2008/0016902 (the '902 Application), which maintained the same title, claims, and inventor as the '921 Application but added to its specification. J.A. 10. On August 7, 2009, the international '902 Application entered the national phase and became US Patent Application 12/526,296 (the '296 Application). *Id.*

information in two paragraphs that appear in the first column. *See id.* col. 1 ll. 15–52.

The specification further describes five methods to explore a potential protective role for the activation of the Nrf2 pathway in neurodegenerative and neuroinflammatory diseases. J.A. 66–67. Methods 1–3 relate to screening, evaluating, and comparing the bioequivalence of compounds for their use against neurological diseases. J.A. 68–69. Methods 4 and 5 relate to the *treatment* of such neurological diseases. J.A. 69. Consistent with the disclosure's original title concerning Nrf2 screening, the totality of the specification focuses primarily on drug discovery. Indeed, the invention's title was only amended to "Treatment for Multiple Sclerosis" in 2011 after Biogen acquired Phase III clinical data for the use of DMF480 in treating MS. *See* J.A. 12–13; J.A. 3490–91.

Because the claims at issue concern methods to treat MS, we must look to methods 4 and 5 as disclosed in the specification. Method 5 is largely irrelevant for our purposes because it relates to combination therapy comprising the administration of a compound that upregulates the Nrf2 pathway with at least one other compound that cannot upregulate the pathway. '514 Patent col. 8 ll. 54–63. But method 4 is instructive, as it discloses "methods of treating a neurological disease by administering to the subject in need thereof at least one compound that is at least partially structurally similar to DMF and/or [monomethyl fumarate (MMF)]," as well as "a method of treating a mammal who has or is at risk for a neurological disease . . . [by] administering to the mammal a therapeutically effective amount of at least one neuroprotective compound" such as DMF or MMF, and "a method of slowing or preventing neurodegeneration" induced by demyelination or the death or neurons. *Id.* col. 8 ll. 35–53.

Save for one paragraph in the specification, the disclosure does not teach potential dosage levels for DMF

monotherapy. The sole DMF-dosage paragraph is not linked to treatment of any specific disease but recites:

> Effective doses will also vary, as recognized by those skilled in the art, dependent on route of administration, excipient usage, and the possibility of co-usage with other therapeutic treatments including use of other therapeutic agents. For example, an effective dose of DMF or MM[F] to be administered to a subject orally can be from about 0.1 g to 1 g per pay, 200 mg to about 800 mg per day (e.g., from about 240 mg to about 720 mg per day; or ***from about 480 mg to about 720 mg per day***; or about 720 mg per day). For example, the 720 mg per day may be administered in separate administrations of 2, 3, 4, or 6 equal doses.

*Id.* col. 18 ll. 54–64 (emphasis added). As shown above, the specification explicitly mentions "effective doses" at various concentration ranges within an overall DMF dosage range of 100–1,000 mg/day.

Importantly for this appeal, the specification reveals two crucial aspects of the invention. First, the above paragraph features the *one and only* reference to DMF480 in the entire specification, which puts the DMF480 dose that the '514 Patent claims at the bottom end of the spectrum of a DMF 480–720 mg/day range. Second, the specification defines the term "effective" within a therapeutic, rather than drug-discovery, context. Thus, according to the specification, the terms "'therapeutically effective dose' and 'therapeutically effective amount' refer to that amount of a compound which results in at least one of *prevention* or *delay* of onset or *amelioration of symptoms* of a neurological disorder in a subject or an attainment of a *desired biological outcome, such as reduced neurodegeneration* (e.g., demyelination, axonal loss, and neuronal death) or *reduced inflammation* of the cells of the CNS." *Id.* col. 5 ll. 52–59 (emphases added).

B. Clinical Development and Procedural History

Between 2004 and 2006, Biogen conducted a Phase II, clinical, dose-ranging study to test the efficacy of DMF at 120, 360, and 720 mg/day concentrations (DMF120, DMF360, and DMF720, respectively) for the treatment of MS. J.A. 2184–91. The May 2006 results of this study showed that DMF720 was efficacious in treating MS, but DMF120 and DMF360 were not. J.A. 7. In August 2006, the FDA recommended that Biogen add a DMF480 dosing regimen in the Phase III study because the lower dose "might improve patient compliance and/or minimize drop-outs from adverse effects during the study." J.A. 1724–25. According to Biogen, the Phase II lead scientist, Dr. O'Neill, had conceived the idea of using DMF480 as early as 2003 and advocated testing the DMF480 dose as part of the trial in February 2004. J.A. 7. At the time, Biogen had decided not to include the DMF480 dose in the study for commercial reasons. *See* J.A. 1364. Although Biogen told the FDA that DMF720 was the best option, it eventually included DMF480 in the Phase III clinical testing. *See* J.A. 1726. The Phase III results showed efficacy for the DMF480 and DMF720 doses. J.A. 2060.

Based on the 2006 Phase II results—and before starting the Phase III trial to test the DMF480 dose—Biogen filed the provisional '921 Application on February 8, 2007. The original application listed Dr. Lukashev, a Biogen scientist who, at the time, focused on research related to the Nrf2 pathway, as the sole inventor. J.A. 8–10. O'Neill was not listed as a co-inventor on the '921 Application; his name was added in 2011 as part of an amendment refocusing the invention on methods of treatment for MS, which Biogen filed after gathering the Phase III results that demonstrated therapeutic efficacy of DMF480.[4] J.A. 3437–39;

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[4] Biogen amended the '296 Application—the national-phase application filed in 2009, *see supra* note 3—

J.A. 3481–86. O'Neill, however, had not been involved with any of the Nrf2 research that led to the '514 Patent. When asked during trial, Lukashev testified that he did not know why O'Neill was added as an inventor. J.A. 1318. Lukashev also corroborated the original application's emphasis on drug discovery by noting that his work had encompassed "a more exploratory nature. It[ was] to explore potential for follow-on compound discovery . . . ." J.A. 9 (alteration in original). And, more importantly, he "denied that his research could be extrapolated to a clinical dose of DMF; it 'was never the focus of [his] work to inform the clinical dosing of [DMF].'" *Id.* (alterations in original). Besides the amendments related to inventorship and the invention's title, Biogen did not make any other changes to the specification. This enabled Biogen to claim a priority date of February 8, 2007, despite filing wholly new claims alongside the amendments. J.A. 13.

In 2017, Biogen filed its patent infringement suit against Mylan in the Northern District of West Virginia. J.A. 6001. Biogen sued after Mylan sought ANDA approval to market a generic DMF product for treating MS. Mylan counterclaimed for declaratory judgment that the '514 Patent was invalid and not infringed. J.A. 6136–44.

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after acquiring its Phase III clinical-data results in April 2011. J.A. 10. Biogen left the specification of the '296 Application unchanged, but it amended the invention's title and claims on June 20, 2011. J.A. 47. On October 28, 2011, Biogen subsequently amended the '296 Application again to add O'Neill as an inventor. *Id.* Biogen then abandoned the '296 Application in favor of US Patent Application 13/326,426 (the '426 Application), a continuing application filed on February 13, 2012. J.A. 11. The '426 Application eventually led to issuance of the '514 Patent on March 19, 2013. *Id.* Biogen claims a February 8, 2007 priority date for the '514 Patent based on the '921 Application. *Id.*

The district court held a four-day bench trial starting on February 4, 2020. J.A. 1001. On February 5, 2020, the Patent Trademark and Appeal Board (Board) issued a final written decision in a related inter partes review (IPR) proceeding, which Mylan initiated on July 13, 2018 and is the subject of a companion case to this appeal. *See Mylan Pharms. Inc. v. Biogen MA Inc.*, No. IPR2018-01403, 2020 WL 582736 (P.T.A.B. Feb. 5, 2020). In the IPR case, the Board rejected an obviousness challenge to the asserted '514 Patent claims, which estopped Mylan from litigating obviousness issues in the trial court. *See* J.A. 3 n.2.

During trial, the parties agreed that, for purposes of this case, a person of ordinary skill in the art (POSA) is someone with "at least a medical degree, at least three years of training in neurology, and at least three years of clinical experience treating multiple sclerosis patients." J.A. 20. The parties presented expert testimony from two neurologists who treat patients with MS—Dr. Greenberg for Mylan and Dr. Wynn for Biogen. J.A. 20. At the conclusion of the trial, the district court found that the specification did not reasonably convey to a POSA that the '514 Patent inventors had "actually invented" a method of treating MS with a therapeutically effective dose of DMF480 as of February 8, 2007. J.A. 45. The court also found that Biogen's arguments and Wynn's testimony that a POSA would be drawn to the DMF480 dose upon reading the patent specification were "neither credible nor persuasive," J.A. 30–31, and noted that Wynn conceded during cross examination that the sole DMF-dosage paragraph in the specification did not teach a POSA that DMF480 would be therapeutically effective for treating MS, J.A. 31.

The district court opined that Biogen's attempt to "combin[e] a few selectively[ ]plucked disclosures from the specification . . . has been squarely rejected by the Federal Circuit." J.A. 45. Based on the testimony offered at trial, the context of the '514 Patent prosecution history, and "significant omissions from the specification," the district court

ultimately concluded that Mylan had satisfied its burden of showing by clear and convincing evidence that the asserted '514 Patent claims were invalid for lack of written description under 35 U.S.C. § 112. *Id.* Biogen now appeals the district court's decision.

## II. STANDARD OF REVIEW

Whether a claim meets the written-description requirement is a question of fact, which this court reviews for clear error on appeal from a bench trial. *Nuvo Pharm. (Ireland) Designated Activity Co. v. Dr. Reddy's Laboratories Inc.*, 923 F.3d 1368, 1376 (Fed. Cir. 2019), *cert. denied*, 140 S. Ct. 902 (2020). The clear-error standard requires courts to exercise deference when reviewing findings of fact, unless there is a "definite and firm conviction that a mistake has been made." *Scanner Techs. Corp. v. ICOS Vision Sys. Corp. N.V.*, 528 F.3d 1365, 1374 (Fed. Cir. 2008) (internal quotation marks and citation omitted). Patent invalidity under the written-description doctrine must be established by clear and convincing evidence. *Hynix Semiconductor Inc. v. Rambus Inc.*, 645 F.3d 1336, 1351 (Fed. Cir. 2011). Courts of appeals cannot reweigh a district court's assessment of witness credibility, *Advanced Magnetic Closures, Inc. v. Rome Fastener Corp.*, 607 F.3d 817, 832 (Fed. Cir. 2010), and must take into account the "unchallenged superiority" of a district court's ability to make witness-credibility determinations and findings of fact, *see Salve Regina Coll. v. Russell*, 499 U.S. 225, 233 (1991).

## III. DISCUSSION

### A. The Written-Description Requirement

To secure a patent for an invention under the laws of the United States, an inventor must comply with the written-description requirement outlined in 35 U.S.C. § 112, which prescribes:

> The [patent] specification shall contain a *written description* of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.[5]

35 U.S.C. § 112 (emphasis added). The statutory mandate for a written description as a prerequisite for patenting an invention has been a fixture of our laws for more than two centuries. The Supreme Court recognized, as far back as 1822, that the purpose of requiring a written description under the Patent Act of 1793 was to "put the public in possession of what the party claims as his own invention, so as to ascertain if he claim[s] anything that is in common use, or is already known . . . ." *Evans v. Eaton*, 20 U.S. 356, 434 (1822). "[P]ossession as shown in the disclosure," therefore, represents the hallmark of written description. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). The written-description statutory language has undergone little change despite the enactment and revisions of numerous patent statutes since the Founding era. *See Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 925 (Fed. Cir. 2004).

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[5] Following the enactment of the Leahy–Smith America Invents Act (AIA), Pub. L. No. 112-29, 125 Stat 284 (2011), the first paragraph of § 112 was redesignated as § 122(a). The AIA amendments, which took effect on September 16, 2012, replaced the words "of carrying out his invention" in the pre-AIA § 112 with "or joint inventor of carrying out the invention" in the current § 112(a). 125 Stat. at 296–97. The amendments bear no significance for purposes of our written-description analysis.

This court's precedents dictate that the § 112 written-description "requirement is satisfied only if the inventor 'convey[s] with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention,' and demonstrate[s] that by disclosure in the specification of the patent." *Nuvo*, 923 F.3d at 1376–77 (quoting *Centocor Ortho Biotech, Inc. v. Abbott Laboratories*, 636 F.3d 1341, 1348 (Fed. Cir. 2011)). A precise definition of the invention is pivotal to establishing possession. *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1373 (Fed. Cir. 2017). An applicant may show possession of the claimed invention by describing it with all of its limitations using "such descriptive means as words, structures, figures, diagrams, formulas, etc." *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). The term "possession" in the context of written-description jurisprudence entails an "objective inquiry into the four corners of the specification from the perspective of a [skilled artisan]." *Ariad*, 598 F.3d at 1351.

Whether a claimed invention satisfies the written-description requirement of § 112 will depend on the nature of the invention. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 963 (Fed. Cir. 2002) (citations omitted). Thus, the written-description analysis is highly dependent on the facts of each case. *Nuvo*, 923 F.3d at 1383 (citations omitted). In general, "written description is judged based on the state of the art as of the priority date. . . . [E]vidence illuminating the state of the art subsequent to the priority date is not relevant to written description." *Amgen*, F.3d at 1373–74 (internal citation omitted).

B. Possession of the Claimed Invention

The core issue in this appeal is whether the specification Biogen filed on February 8, 2007 supports the 2011 claims that issued in the '514 Patent. Even more precisely, the narrow ground on which this question turns is whether the original specification describes "possession" of the

claimed therapeutically effective DMF480-dose limitation to treat MS.

The district court began by properly noting that "it is the specification itself that must demonstrate possession." J.A. 23 (quoting *Ariad*, 598 F.3d at 1352). The specification covers a broad array of nearly three dozen neurological disorders, and MS may arguably constitute an important element of the disclosure from the start. *See* '514 Patent col. 1 ll. 12–52 (explaining that the overall purpose of the invention is to treat "demyelinating neurological diseases," such as MS). Next, DMF appears more than two-dozen times throughout the specification, including in the three examples listed in the disclosure. The prior art demonstrates the existence of a link between DMF-mediated activation of the Nrf2 pathway and the neuroprotective and therapeutic effects of said activation, which could be exploited for the treatment of certain neurological disorders such as MS. *See id.* col. 5 ll. 20–24. Thus, assuming that a skilled artisan would understand the disclosure to be unambiguously focused on MS despite its inclusion among approximately three-dozen neurological disorders—a determination we need not reach in this case—the specification may arguably provide adequate information to convey to a skilled artisan that the invention supports method-of-treatment claims directed to MS and, perhaps, that the use of DMF may be therapeutically linked to MS treatment.[6]

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[6] We note, however, that method 4, which is the only relevant method to this appeal, is devoid of any specific reference to MS. *See* '514 Patent col. 8 ll. 35–53; J.A. 27 (noting that MS is merely listed as one of a slew of neurological diseases). The district court further found that Mylan's expert "credibly testified" that nothing in the specification "ties an effective dose of DMF specifically to the treatment of MS." J.A. 29.

The skilled artisan would then look in the specification for guidance vis-à-vis a suitable therapeutic-DMF dosage. This is where the district court noted the lack of written description, upon which it primarily based its finding of invalidity. The DMF480 dose is listed only once in the entire specification. *See* '514 Patent col. 18 l. 62. The specification's sole reference to DMF480 constitutes a significant fact that cuts against Biogen's case, particularly because it appears at the end of one range among a series of ranges, including DMF concentrations of 100–1,000, 200–800, 240–720, and 480–720 mg/day. That is in stark contrast to DMF720, which is referenced independently as one dose and was known to be effective as of the February 2007 priority date. The '514 Patent, as issued, features multiple claims that are drawn exclusively to the specific DMF480 dose, but the specification's focus on basic research and broad DMF-dosage ranges show that the inventors did not possess a therapeutically effective DMF480 dose at the time of filing in 2007. On this point, Lukashev, the original inventor listed in the '921 Application, offered testimony in which he "denied that his research could be extrapolated to a clinical dose of DMF; it 'was never the focus of [his] work to inform the clinical dosing of [DMF].'" J.A. 9 (alterations in original); *see also* J.A. 34 (noting that the district court found Lukashev's testimony credible as to the fact that all the examples listed in the specification were part of his research and would not have been "helpful in identifying a therapeutically effective" DMF dose). Likewise, the district court credited Mylan's expert testimony at trial that the paragraph containing the sole DMF480 reference fails to specifically link an effective dose of DMF to the treatment of MS. J.A. 29.

This court has previously held that "[s]atisfaction of the description requirement [e]nsures that . . . a claim subsequent to the filing date of the application was sufficiently disclosed at the time of filing so that the prima facie date of invention can fairly be held to be the filing date of the

application." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1562 (Fed. Cir. 1991) (quoting *In re Smith & Hubin*, 481 F.2d 910, 914 (CCPA 1973)). An inventor need not "prove that a claimed pharmaceutical compound actually achieves a certain result. But when the inventor expressly claims that result, our case law provides that [such] result must be supported by adequate disclosure in the specification." *Nuvo*, 923 F.3d at 1384. Based on the evidence in the record, the district court did not clearly err in determining that Mylan established its burden of showing, by clear and convincing evidence, that the specification does not adequately support the asserted claims of the '514 Patent. More specifically, the district court did not clearly err in finding that a skilled artisan would not have recognized, based on the single passing reference to a DMF480 dose in the disclosure, that DMF480 would have been efficacious in the treatment of MS, particularly because the specification's only reference to DMF480 was part of a wide DMF-dosage range and not listed as an independent therapeutically efficacious dose.

That Biogen later established the therapeutic efficacy of DMF480 is of no import to the written-description analysis. What matters for purposes of the inquiry in this case is whether, at the time of filing the disclosure—well before the Phase III study even commenced—a skilled artisan could deduce simply from reading the specification that DMF480 would be a therapeutically effective treatment for MS. As to this point, the specification's focus on drug discovery and basic research further buttresses the district court's conclusion that the specification lacks an adequate written description to support the DMF480 claims. At the time of filing the original disclosure in 2007, the Nrf2 insights that proved critical in the Phase III study had not yet been translated to clinical use. *See* J.A. 35 (finding that, based on the evidence presented at trial, Lukashev's research related to Nrf2 activation and small-molecule screening "had nothing to do with the clinical development

of Tecfidera®"). Regardless of whether O'Neill had in fact hypothesized or even conceived the idea of treating MS with a DMF480 dose as early as 2003, *see* J.A. 1586–87, the law is clear that a patent cannot be awarded for mere theoretical research without more, *see Ariad*, 598 F.3d at 1353. The written-description requirement limits patent protection only to individuals who perform the difficult work of producing a complete and final invention featuring all its claimed limitations and publicly disclose the fruits of that effort. *Id.* We therefore determine that, based on the evidence in the record, the district did not clearly err in finding that Biogen did not possess an invention directed to the specific use of a therapeutically effective DMF480 dose for the treatment of MS as of 2007.

Confronted with the lack of a specific reference to DMF480, Biogen and its expert argued that a skilled artisan would be drawn to the DMF480 dose because it was "anchored" to the effective DMF720 dose. J.A. 1548–49. But the very same sentence in the specification that discloses the DMF 480–720 mg/day range also "anchors" DMF240 (a known ineffective dose) to DMF720 (according to the DMF 240–720 mg/day range). *See* '514 Patent col. 18 ll. 54–64. Not only does the specification anchor an ineffective dose, it also expands the purported range of therapeutic efficacy from DMF100 and DMF200 (doses that a skilled artisan would expect to be ineffective) to DMF1,000 (a dose well above the therapeutically effective DMF720 mg/day dose). *See id.* col. 18 ll. 54–64; Appellee's Br. 26. That column 18 of the '514 Patent specification recites several DMF doses in the 100–1,000 mg/day range as "effective" without even identifying a target disease is further indicative that the inventors were not in possession of a complete and final invention as of February 2007.

Lastly, the court noted that Mylan had impeached Wynn's credibility by pointing out his inconsistent statements and evasiveness when asked, during the district court proceedings, why a skilled artisan would be drawn to

the purported DMF480 efficacy upon reading the patent specification—all while consistently maintaining that a skilled artisan would not have reasonably expected DMF480 to provide the therapeutic efficacy claimed in the patent during the IPR proceeding. J.A. 31–33. After hearing live testimony from the parties' experts at trial, the district court found that the Biogen expert's opinion that a skilled artisan would be drawn to a DMF480 dose was "neither credible nor persuasive." JA 30–31. We discern no principled reason to disturb the district court's assessment as to the credibility of Biogen's expert testimony. *See Salve Regina Coll. v. Russell*, 499 U.S. 225, 233 (1991) (describing the "unchallenged superiority" of a district court as to the assessment of witness credibility and making findings of fact); *Highmark, Inc. v. Allcare Health Mgmt. Sys., Inc.*, 701 F.3d 1351, 1366 (Fed. Cir. 2012) (Reyna, J., dissenting from the denial of the petition for rehearing en banc) (noting that intervention as to issues of fact finding should be limited to instances of clear error, especially given that "an appellate court cannot adequately, if at all, assess credibility of [expert] testimony because the witness is not before [the appellate panel] in person.").

Viewing the record before us in its totality, we discern no clear error in the district court's judgment that Mylan established its burden of showing, by clear and convincing evidence, that the asserted '514 Patent claims are invalid for lack of written description under 35 U.S.C. § 112.

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Biogen raises several ancillary issues in an effort to reverse the district court decision. For example, Biogen claims that the district court "misinterpret[ed] this [c]ourt's 'blaze[-]marks' jurisprudence; fail[ed] to consider the specification as a whole; erroneously appl[ied] judicial estoppel; disregard[ed] the specification's express disclosure of the claimed dose because it was not described as the most preferred; and confus[ed] the written-description

requirement with principles of obviousness and unexpected results." Appellant's Br. 2. But our conclusion that the district court did not clearly err in finding the '514 Patent invalid for lack of written description under § 112 renders all these arguments superfluous.

Notably, the Dissent claims that the district court legally erred by conflating therapeutic and clinical efficacy. *See* Dissent Op. at 6, 8. However, when viewed through the lens of the '514 Patent, this is not a legal issue, but a factual one. The district court, as the finder of fact, did not find it necessary or appropriate to distinguish between therapeutic effects and clinical efficacy based on the specification's definition of "therapeutically effective dose" and the record before it, and such a determination was not clearly erroneous.

Most notably, the specification's definition of "therapeutically effective dose" indisputably features both clinical and therapeutic insignia. For example, the specification defines a "therapeutically effective dose" as an "*amount* of a compound" that results in the "prevention or delay of onset or amelioration of *symptoms of a neurological disorder in a subject*," namely, clinical insignia, "or an attainment of a *desired biological outcome*, such as reduced neurodegeneration (e.g., demyelination, axonal loss, and neuronal death) or reduced inflammation of the cells of the CNS," which constitute therapeutic insignia. '514 Patent col. 5 ll. 52–59 (emphases added).

On redirect examination, Biogen's expert attempted to characterize the specification's definition as solely describing therapeutic effects—"demyelination, axonal loss, and neuronal death" as well as "fewer [brain] scars"—that once could "see on [an] MRI scan, for example." J.A. 1553–54. He distinguished these from clinical endpoints, such as "a person hav[ing] less episodes" or "no[ ] progression" of *symptoms*, including "weakness, numbness, loss of bladder or bowel control, [sight deterioration], [and] less relapses."

J.A. 1553. But Biogen's expert did not explain why these improved clinical outcomes would not qualify under the first half of the specification's definition, which focuses on preventing, delaying the onset of, or ameliorating "*symptoms of a neurological disorder*" in patients. '514 Patent col. 5 ll. 52–55 (emphasis added).

Based on the record, including at least the specification's definition of a "therapeutically effective dose" and the witness and expert testimony, the district court did not find it necessary to distinguish between therapeutic effects and clinical efficacy with respect to its patentability determination, instead electing to consider both under the specification's definition of "therapeutically effective dose." We determine that such a finding was not clearly erroneous.

Accordingly, we conclude that the district court did not clearly err in determining that the original 2007 disclosure, which focused exclusively on screening compounds for activation of the Nrf2 biological pathway, did not disclose a method to administer a therapeutically effective dose of DMF480 for the treatment of MS. Nor did the district court clearly err in finding that "O'Neill's hypothesis, that a [DMF480 dose] would be efficacious in treating MS, evolved from his review" of confidential information, which a skilled artisan would not have been privy to in 2007 and was never included in the original disclosure. *See* J.A. 35, 42, 1586–87.

Because we hold that the '514 Patent is invalid under the written-description doctrine, we need not reach the merits of the parties' arguments in the companion IPR case.

## IV. CONCLUSION

For the reasons set forth in this opinion, we affirm the district court's decision that Mylan satisfied its burden of showing, by clear and convincing evidence, that the asserted '514 Patent claims are invalid for lack of written

description under 35 U.S.C. § 112. Viewed in its totality, the record shows that the inventors were not in possession of a method of administering a therapeutically effective dose of DMF480 to treat MS on or before the February 8, 2007 priority date. We have considered the parties' remaining arguments and find them unavailing or do not reach them.

**AFFIRMED**

# United States Court of Appeals for the Federal Circuit

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**BIOGEN INTERNATIONAL GMBH, BIOGEN MA, INC.,**
*Plaintiffs-Appellants*

**v.**

**MYLAN PHARMACEUTICALS INC.,**
*Defendant-Appellee*

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2020-1933

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Appeal from the United States District Court for the Northern District of West Virginia in No. 1:17-cv-00116-IMK-JPM, Judge Irene M. Keeley.

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O'MALLEY, *Circuit Judge*, dissenting.

While I am loath to reverse district court determinations that rely heavily on credibility findings, I must respectfully dissent. There is no dispute over whether the district court erred in finding that Biogen was judicially estopped from drawing a distinction between clinical and therapeutic effects: it did. Mylan calls the error harmless and the majority finds it "ancillary" to its analysis. I, on the other hand, believe this threshold error impacted the district court's entire written description analysis. I would therefore reverse and remand for reconsideration in light of a proper understanding of the distinction between the two effects and the written descriptions needed for each.

I.

A. The district court erred in applying judicial estoppel

As it had tried to do throughout the trial, Biogen explained the distinction between *clinical efficacy* and *therapeutic effects* in its post-trial briefs before the district court. Clinical efficacy involves the type of scientific rigor associated with Phase III clinical trials: the investigative DMF480 dose must produce superior clinical endpoints to the standard of care for MS, Rebif®. *See* J.A. 8066. Therapeutic effects, by contrast, "do not require efficacy on clinical endpoints or superior efficacy to existing drugs." *Id.* It, instead, "refer[s] to the amount of [DMF480] which results in . . . prevention or delay of onset or amelioration of symptoms of a neurological disorder" like MS. '514 patent, col. 5, ll. 52–55.

Based on this distinction, Biogen took issue in its post-trial brief with Mylan's contention that the '514 patent lacked written description support because "a person of ordinary skill in the art would not have a reasonable expectation that the 480 mg/day [DMF] dose would provide statistically significant and clinically meaningful effectiveness for treating MS." J.A. 8064 (citing Mylan's post-trial brief, which quoted Dr. Dawson's testimony). Biogen pointed out that, in addition to mixing up written description and obviousness inquiries (which I will discuss *infra*), Mylan's argument erroneously assumed that the claims required *clinical* efficacy when they only covered *therapeutic* effects. J.A. 8063–66.

In a two-sentence footnote, the district court concluded that Biogen was judicially estopped from pointing out the distinction between clinical and therapeutic efficacy. *Biogen Int'l GmbH v. Mylan Pharms. Inc.*, 2020 WL 3317105, at *8 n.15 (N.D.W. Va. June 18, 2020). Citing *New Hampshire v. Maine*, 532 U.S. 742 (2001), the district court reasoned that Biogen could not "deliberately chang[e] positions according to the exigencies of the moment." *Id.*

I need not detail why the court's footnote ruling on judicial estoppel constituted an abuse of discretion under Fourth Circuit law. *See Martineau v. Wier*, 934 F.3d 385, 393 (4th Cir. 2019) (setting out a multi-factor test for the judicial estoppel inquiry, which the district court wholly failed to apply in this case). Biogen's briefs explain this error in detail and neither Mylan nor the majority defends the district court's ruling under that governing law.

I will, however, provide detail on how the erroneous judicial estoppel ruling led the district court to legally err in its interpretation of Federal Circuit written description precedent. In my view, the district court's refusal to acknowledge the difference between *therapeutic* and *clinical* effects evinces a fundamental misunderstanding of what is claimed—and, thus, what requires written description support—in the '514 patent.

The '514 patent explains that neurodegenerative disorders like MS are "characterized by inflammation in parts of the [central nervous system (CNS)], leading to the loss of the myelin sheathing around neuronal axons (demyelination), loss of axons, and the eventual death of neurons, oligodendrocytes and glial cells." '514 patent, col. 1, ll. 17–20. The '514 patent discusses the promise of treating MS using DMF, "a member of a large group of anti-oxidant molecules known for their cytoprotective and anti-inflammatory properties." '514 patent, col. 5, ll. 16–18. The '514 patent claims a "therapeutically effective amount" of DMF480, which the specification defines as

> that amount of a compound which results in at least one of prevention or delay of onset or amelioration of symptoms of a neurological disorder in a subject or an attainment of a desired biological outcome, such as reduced neurodegeneration (e.g., demyelination, axonal loss, and neuronal death) or reduced inflammation of the cells of the CNS.

'514 patent, col. 5, ll. 52–59.

Notably, the '514 patent explains that the inventors measured DMF's *therapeutic* efficacy in terms of its ability to enhance the expression levels of Nrf2—a transcription factor that activates the expression of genes responsible for protecting cells from the neurodegeneration commonly associated with MS. *See* '514 patent, col. 5, ll. 16–24; *see also* '514 patent, col. 1, ll. 35–62. Figures 3 and 4 of the '514 patent provide *in vivo* data showing an increase in Nrf2 expression following DMF treatment. '514 patent, Figures 3 and 4; *see also* '514 patent, col. 22, ll. 1–13. And, the '514 patent states: "the finding that *DMF activates the Nrf2 pathway* . . . offers a rationale for identification of structurally and/or mechanistically related molecules that would be expected to be *therapeutically effective* for the treatment of neurological disorders, such as, e.g., MS." '514 patent, col. 5, ll. 19–24 (emphasis added). Taken together, it is clear on the face of the '514 patent that the claimed "*therapeutically* effective amount" refers to DMF's ability to mitigate MS symptoms vis-à-vis its modulation of Nrf2 expression; it has nothing to do with whether DMF480 outperforms the standard of care for MS (Rebif®) in a Phase III clinical trial setting.

It is no wonder, then, why Biogen—in response to Mylan's repeated contentions that the '514 patent fails the written description requirement because it lacks Phase III *clinical* efficacy data—sought in its post-trial briefing to remind the district court that the written description inquiry should focus on *therapeutic* efficacy.[1] Far from deliberately changing positions as the district court accused it of, Biogen was simply attempting to direct the district court's attention to the claim language at issue. Judicially estopping Biogen from doing so was not just legally erroneous under

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[1] To be sure, Mylan continues its erroneous conflation of therapeutic and clinical efficacy before our court. *See, e.g.*, Appellee's Resp. Br. at 48–49.

Fourth Circuit law, it misapplied our written description precedents by ignoring the claims at a time when they should have been given primacy. *Cf. Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) ("It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude.") (citations omitted) (internal quotation marks omitted).[2]

As discussed further below, the impact of the district court's errant refusal to acknowledge the difference between *therapeutic* and *clinical* efficacy is evident throughout the rest of the opinion.

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[2] The majority's argument that there is no ascertainable difference between clinical and therapeutic efficacy is wrong for several reasons. *See* Maj. Op. at 20–21. As I have detailed above, the '514 patent makes clear that "therapeutically effective amount" does not involve comparing the claimed DMF480 dosage to the standard of care for MS like a clinical trial would. And, neither party ever argued this—either to the district court or on appeal. Biogen, instead, advocated distinguishing the two while Mylan and the district court blithely proceeded as though there were no difference without ever providing any explanation. To make up for this deficiency in the trial record, the majority provides its own explanation: "clinical insignia" is somehow encompassed by the '514 patent's definition of "therapeutically effective dose." *Id.* (citing '514 patent, col. 5, ll. 52–59). The majority appears to forget our role in this appeal: we are a court of review, not the primary factfinder. To the extent the majority fashions its own explanation of why therapeutic and clinical efficacy are one in the same, it crosses that line.

B. The district court's conflation of therapeutic and clinical efficacy caused it to erroneously require clinical data, rather than therapeutic effects

The district court's failure to distinguish therapeutic effects and clinical efficacy also led it to conflate concepts of obviousness and written description. This conflation, in my view, caused the district court to erroneously require a showing of clinical data akin to what would be gathered in Phase III clinical trials in its written description analysis.

Somewhat circularly, after acknowledging that clinical data demonstrating effectiveness is not required to satisfy written description, the district court went on to find that the '514 patent does not demonstrate possession because it lacks clinical efficacy data. *Biogen*, 2020 WL 3317105, at *15. To arrive at this conclusion, the district court relied on its interpretation of our precedent in *Nuvo*. According to the district court, the patentees in *Nuvo* could not establish possession because a POSA "would not have expected [the claimed drug] to be effective, and nothing in the specification would teach a [POSA] otherwise." *Id.* (quoting *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy's Lab'ys Inc.*, 923 F.3d 1368, 1377, 1381 (Fed. Cir. 2019) (alteration in original). The district court reasoned that the same set of facts are at issue in this case: because Biogen had defended against Mylan's obviousness challenges in this case and a related *inter partes* review proceeding by contending that a POSA would not have expected the DMF480 dose to *clinically* treat MS, the '514 patent's failure to teach a POSA otherwise with clinical data dooms Biogen's written description arguments. *Id.* (citing *Nuvo*, 923 F.3d at 1381).

This cannot be right. Whether a claim satisfies the written description requirement of § 112 is a question of fact that we review for clear error. *Ariad Pharms. v. Eli Lilly and Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010). We provide de novo review, however, of a district court's

interpretation of Federal Circuit precedent. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1337 (Fed. Cir. 2003). Our court has long held that "the hallmark of written description is disclosure," meaning that a patent must "reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351.

Here, the district court's reading of *Nuvo* does not accurately describe what we actually held in that case. The patent at issue in *Nuvo* claimed an acid inhibitor that was *uncoated* and *effective* at raising pH levels. *Nuvo*, 923 F.3d at 1373–1374, 1378. The patent specification in *Nuvo*, however, specifically discussed a known problem in the prior art involving *uncoated* acid inhibitors' *ineffectiveness* at raising pH levels. *See id.* at 1375 (reversing the district court for "not explain[ing] why the mere disclosure of [uncoated acid inhibitors], coupled with the known disadvantages of coated [acid inhibitors], is relevant to the therapeutic effectiveness of uncoated [acid inhibitors], *which the patent recognized as problematic for efficacy due to its potential for destruction by stomach acid*") (emphasis added). Since the patentees in *Nuvo* did nothing to explain how the invention purported to overcome the commonly known problem with *uncoated* formulations that the patent specification explicitly discussed, our court invalidated the patent for lack of written description. *Id.* at 1381. Nowhere in *Nuvo* did we overlay a POSA's reasonable expectation of success from the obviousness context onto the written description inquiry. To the extent *Nuvo* mentioned a POSA's expectations, it cabined this discussion to what a POSA would have expected based on the explicit teachings of the patent specification—not of the prior art. *See id.* at 1381 ("In light of the fact that the specification provides nothing more than the mere claim that uncoated [acid inhibitors] might work, even though persons of ordinary skill in the art would not have thought it would work, the specification is fatally flawed.").

The district court's reliance on *Nuvo* to conclude that Mylan could use Biogen's own obviousness defenses against it in the written description context is, therefore, legally erroneous. What a POSA would expect regarding clinical efficacy based on the prior art is a distinct question from whether a POSA would understand that the inventor possessed the *claimed* invention—i.e., a therapeutically effective dose—based on the patent's written description. Since the district court never engaged in a proper written description inquiry, I would reverse and remand for further proceedings consistent with a proper written description analysis that minds the gaps between obviousness and written description, as well as therapeutic and clinical efficacy.[3]

C. The district court's conflation of therapeutic and clinical efficacy caused it to erroneously apply our "blaze marks" precedent

The majority relieves me of the need to discuss the district court's erroneous conclusion that the '514 patent does not contain enough "blaze marks" to direct a POSA toward MS treatment. *See Biogen*, 2020 WL 3317105, at *10 ("Method 4 broadly describes treating neurological diseases with a therapeutically effective amount of DMF; MS is merely one such disease 'among a slew of competing possibilities.'") (citing *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013)). The majority opinion—appearing to recognize this obvious

[3] To the extent the majority accuses the dissent of reweighing the district court's credibility determinations, I disagree. *See* Maj. Op. at 19–20. Because I believe the district court's misguided interpretation of *Nuvo* led it to erroneously require clinical efficacy data for the written description inquiry, any expert witness testimony on which the district court relied to bolster that requirement is also legally unsound.

error—says it operates under the assumption that the '514 patent satisfies written description in this regard. Maj. Op. at 15–16. Given the specification's repeated references to MS, that is a wise decision on the majority's part.

I do, however, need to discuss the district court's finding (an erroneous one, in my view) that the '514 patent does not contain enough "blaze marks" to "'link' a therapeutically effective amount of DMF to a dose of 480mg/day." *Biogen*, 2020 WL 3317105, at *10. The district court cites our precedent in *Ariad*, as well as Dr. Greenberg's trial testimony, to justify its application of our "blaze marks" precedent to this case. *Id.* I do not believe our case law required these patentees to include "blaze marks" in the '514 patent, however. And, the district court's reliance on Dr. Greenberg's testimony to conclude that the patentees should have included "blaze marks" only perpetuated its legally erroneous interpretation of our case law. *See* J.A. 1447–49.

It is axiomatic that, to satisfy the written description requirement, a patent specification must "clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad*, 598 F.3d at 1351 (citations omitted) (alteration in original). This fundamental concept gets tested, however, whenever a patent's specification discloses a broad genus and claims a particular species contained within that genus. In cases such as these, our court has crafted a subgenre within our written description jurisprudence that requires patents containing laundry list-type disclosures "to provide sufficient 'blaze marks' to guide a reader through the forest of disclosed possibilities toward the claimed compound." *Novozymes*, 723 F.3d at 1346; *see also In re Ruschig*, 379 F.2d 990, 994–995 (C.C.P.A. 1967) ("It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail or in finding one's way through the woods where the trails have disappeared . . . to be confronted simply by a large number of unmarked trees."). Notably, our "blaze marks" jurisprudence does not apply in *every*

case concerning written description; it, instead, provides a useful framework to analyze whether written description has been met in cases involving patents containing laundry list disclosures. *See, e.g.*, *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571 (Fed. Cir. 1996) ("In the absence of such blazemarks, simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or sub-genuses.").

On my reading of the '514 patent, the district court erred as a matter of law by requiring Column 18 to contain sufficient "blaze marks" regarding the claimed DMF480 therapeutically effective dose. Method 4 of the '514 patent provides a general discussion of treating neurological diseases, such as MS, with therapeutically effective amounts of DMF compounds. *See* '514 patent, col. 8, ll. 35–53. Column 18 picks up where Method 4 left off by indicating which specific DMF doses the patentees considered therapeutically effective. *See id.*, col. 18, ll. 52–64. Column 18 does this by providing ranges of DMF doses—some large, *see id.* at col. 18, ll. 58–60 ("0.1 g to 1 g per [d]ay"), and some small, *see id.*, col. 18, l. 61 ("240 mg to about 720 mg per day"). Notably, Column 18 contains an express disclosure of the claimed DMF480 dose[4]; this reference also comes in

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[4] The majority's decision affirming the district court partially rests on the fact that the '514 patent only mentions the claimed DMF480 dose once. Maj. Op. at 16. But the majority cites no case law (and I know of none) for the proposition that the written description requirement demands that a patentee recite a claim element repeatedly to pass written description muster. The majority does not, and cannot, deny that the claimed DMF480 dose is expressly disclosed. To the extent the majority's opinion may be read to establish a requirement that a claim element must be disclosed multiple times, I dissent from that holding as well.

the form of a range. *See id.* at col. 18, l. 62 ("480 mg to about 720 mg per day.").

I do not believe our "blaze marks" precedent applies to the claimed DMF480 dose because Column 18 does not provide a laundry list disclosure of therapeutically effective doses. Despite providing a varying degree of ranges, Column 18 begins one such range with the *exact* DMF480 dose that is claimed. *See id.* Had the patentees instead listed this range as, e.g., "*100 mg* to about 720 mg per day" and expected a POSA to figure out that a 480 mg per day dose was therapeutically effective, I would agree that "blaze marks" would be necessary to "single out particular trees." *In re Ruschig*, 379 F.2d at 995. But, because the range provided in Column 18 particularly points out the claimed DMF480 dose, I believe the claim satisfies Section 112 and our corresponding written description jurisprudence. The district court's application of our "blaze marks" precedent and corresponding reliance on Dr. Greenberg's testimony thus are erroneous as a matter of law for two reasons. First, as discussed above, our "blaze marks" precedent is not applicable to this case because Column 18 lacks a laundry list disclosure. And, second, even if this precedent were to apply here, Column 18 provides a sufficient "blaze mark" by explicitly mentioning the claimed DMF480 dose. How much brighter need a disclosure blaze?

The district court's inability to "link" method 4 and Column 18, moreover, emanates from its original sin of judicially estopping Biogen from distinguishing between therapeutic and clinical effects. With a proper understanding of this distinction, the written description analysis in this case is straightforward: method 4 provides a general description of treating MS using a therapeutically effective DMF dose and column 18 demonstrates the patentees' possession of the claimed DMF480 dose for that purpose.

## II.

Because I believe the entire course of the district court's analysis might well change if the court were to adjust the lens through which it considers the evidence and testimony, I would remand for reconsideration of the record with the understanding that the patent is not about clinical efficacy—it is about therapeutic effect—and that the written description and obviousness inquiries are not the same.

## CERTIFICATE OF SERVICE

I hereby certify that, on this 30th day of December, 2021, I filed the foregoing with the Clerk of the United States Court of Appeals for the Federal Circuit via the CM/ECF system, which will send notice of such filing to all registered CM/ECF users.

/s/ William F. Lee
WILLIAM F. LEE
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

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/s/ William F. Lee
WILLIAM F. LEE
WILMER CUTLER PICKERING
HALE AND DORR LLP
60 State Street
Boston, MA 02109
(617) 526-6000

December 30, 2021