IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF WEST VIRGINIA

BIOGEN INTERNATIONAL GMBH and
BIOGEN MA, INC.,

Plaintiffs,

v. **CIVIL ACTION NO. 1:17CV116**
(Judge Keeley)

MYLAN PHARMACEUTICALS INC.,

Defendant.

MEMORANDUM OPINION AND ORDER MAKING FINDINGS OF FACT AND GRANTING JUDGMENT IN FAVOR OF THE DEFENDANT, MYLAN PHARMACEUTICALS INC.

I. BACKGROUND

In this patent infringement action, the plaintiffs, Biogen International GmbH and Biogen MA, Inc. (collectively "Biogen"), and the defendant, Mylan Pharmaceuticals Inc. ("Mylan"), dispute whether claims 1-4, 6, 8-13, and 15-16 ("the asserted claims") of Biogen's U.S. Patent No. 8,399,514 ("the '514 Patent") are valid and enforceable (Dkt. Nos. 1 at 14-17, 288 at 1-2).[1] The '514 Patent is associated with Tecfidera®, Biogen's New Drug Application ("NDA") product approved by the FDA for use in the treatment of multiple sclerosis ("MS") (Dkt. No. 1 at 15). Mylan has filed an Abbreviated New Drug Application ("ANDA"), seeking to market a drug that is bioequivalent to Tecfidera®.

[1] All docket and page numbers refer to the numbers assigned by the Court's electronic docket.

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The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (otherwise known as the "Hatch-Waxman Act"), seeks to encourage "pioneering research and development of new drugs," as well as the "production of low-cost, generic copies of those drugs." Eli Lilly & Co. v. Teva Pharm. USA, Inc., 557 F.3d 1346, 1348 (Fed. Cir. 2009). To that end, a manufacturer may obtain Food and Drug Administration ("FDA") approval to market a generic drug by making a certification regarding patents listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations ("the Orange Book") as covering the NDA drug, and certifying that those patents are "invalid or will not be infringed by the manufacture, use, or sale of the new generic drug for which the ANDA is submitted" ("paragraph IV certification"). Id. (citing 21 U.S.C. § 355(j)(2)(A)(vii)(IV)). Upon receiving a paragraph IV certification, a patentee may sue the applicant for patent infringement within 45 days, thus delaying FDA approval of the ANDA. Id. (citing § 355(j)(5)(B)(iii)).

In this case, where Biogen has sued Mylan under the Hatch-Waxman Act for infringement of Tecfidera®, the Court is tasked with deciding whether the asserted claims of Biogen's '514 Patent are

invalid for lack of written description under 35 U.S.C. § 112.[2] As discussed below, the Court **FINDS** that Mylan has demonstrated by clear and convincing evidence that the asserted claims of the '514 Patent are invalid for lack of written description.

II. FINDINGS OF FACT[3]

A. The Parties, Jurisdiction, and Venue

Biogen International GmbH is a corporation organized under the laws of Switzerland with its principal place of business at Landis + Gyr-Strasse 3, 6300 Zug, Switzerland. Biogen MA, Inc. is a corporation organized under the laws of the Commonwealth of

[2] Initially, six patents associated with Tecfidera® were at issue in this case (Dkt. No. 1). On February 5, 2019, the parties stipulated to the dismissal of all claims, counterclaims, and defenses regarding U.S. Patent Nos. 6,509,376; 7,320,999; 7,803,840; and 8,759,393 (Dkt. No. 196). In advance of trial, the parties further stipulated to stay all remaining claims, counterclaims, and defenses regarding U.S. Patent No. 7,619,001 ("the '001 Patent") until June 20, 2020 (Dkt. Nos. 288, 315 at 12, 336 at 44). After the first day of trial, the parties agreed that, based on an intervening decision from the Patent Trial and Appeal Board ("PTAB") in the related inter partes review ("IPR") proceeding, Mylan was collaterally estopped under 35 U.S.C. § 315(e)(2) from asserting its obviousness case under 35 U.S.C. § 103 (Dkt. No. 357 at 3-6). Thus, based on the parties' various stipulations, the only remaining issue at trial was whether the asserted claims of the '514 Patent are invalid for lack of written description under § 112 (Dkt. Nos. 288, 315 at 12, 357 at 3-6).

[3] Further findings of fact regarding matters in dispute are contained in Part III (Discussion).

Massachusetts with its principal place of business at 225 Binney Street, Cambridge, Massachusetts 02142. Mylan is a corporation organized under the laws of West Virginia with its principal place of business at 781 Chestnut Ridge Road, Morgantown, West Virginia 26505. The Court has subject matter and personal jurisdiction, and venue is proper.

B. Factual and Procedural Background

Because the asserted claims of the '514 Patent recite a specific method for treating MS, the Court begins its analysis with a brief discussion of this neurologic disorder, as well as Biogen's clinical development of Tecfidera®, and the relevant prosecution history of Biogen's patent applications related to Tecfidera®.

1. Multiple Sclerosis

MS is a neurologic disorder and autoimmune disease that causes the immune system to attack myelin, a protective sheathing surrounding nerve cell axons (Dkt. Nos. 356 at 106-07, 359 at 84-85). This sheathing protects nerves in the central nervous system, much like a rubber coating protects wires to a computer or stereo system (Dkt. No. 356 at 106-07). Although the immune system is a self-defense system that combats viruses and bacteria that would harm the human body, MS confuses the immune system into attacking

myelin (Dkt. Nos. 356 at 107, 359 at 84-85).[4] This causes inflammation that results in demyelination and leads to axonal loss and death of the nerve cell (Dkt. Nos. 356 at 106-07, 359 at 84-85). Together, this damage results in scarring or lesions on the brain, which can be imaged by magnetic resonance imaging (i.e., an MRI) (Dkt. No. 356 at 112, 359 at 86-87). Those images, in turn, are used to monitor disease progress in patients. Id.

2. Biogen's Due Diligence of Fumapharm AG

Gilmore O'Neill, M.D. ("Dr. O'Neill") is a neurologist specializing in neuromuscular diseases such as MS (Dkt. No. 362 at 109-10). In 2003, while Biogen was negotiating a prospective licensing agreement with Fumapharm AG ("Fumapharm"), a company studying fumarates, Dr. O'Neill participated in a confidential due diligence of Fumapharm (Dkt. No. 362 at 27-28, 52-53; JTX 2133 at

[4] As described by Mylan's expert witness, Benjamin M. Greenberg, M.D., autoimmune diseases such as MS are much like a confused house cat that mistakes a curtain, or other house-hold objects, for an invading mouse (Dkt. Nos. 356 at 107-09). Instead of attacking the mouse, the confused cat attacks a portion of the house it is meant to protect. Id. The cat's breed, and the type of friendly object it attacks, will help identify which autoimmune disease is causing the confusion. Id. For example, a Siamese cat (i.e., multiple sclerosis) may be confused and attack one part of the house (i.e., the central nervous system), and a Tabby cat (i.e., psoriasis) may be confused and attack another part of the house (i.e., the skin). Id. at 107-10.

3-4).[5] This included reviewing confidential studies of Fumaderm® (a mixture of fumarates, including dimethyl fumarate ("DMF")), a drug developed by Fumapharm to treat psoriasis, another autoimmune disease (Dkt. No. 362 at 27-28, 52-53). See supra note 4.

Of significance to the issue at hand, after reviewing these studies and the underlying pharmacology of DMF, Dr. O'Neill hypothesized that the peak level of medication in the blood stream, the "C_{max} of DMF," could be driving the efficacy of DMF (Dkt. No. 362 at 53-54). From this, he conceived the idea that, if the drug's "efficacy might be driven by the maximal exposure of the medicine in the [sic] circulation as opposed to a continuous exposure," a daily dose of 480mg (in two equally divided doses or "BID") of DMF could achieve the correct "maximal exposure" and be efficacious in treating MS (Dkt. No. 362 at 53-54).

3. Biogen's Phase II Development of Tecfidera®

After obtaining a licensing agreement with Fumapharm, Biogen appointed Dr. O'Neill as Medical Director of its BG-12 Development Program (JTX 2133 at 4-5, 9-10, 14),[6] to design and lead the

[5] "JTX" refers to the parties' joint trial exhibits.

[6] BG-12 was Biogen's internal and external name for Tecfidera® prior to its receipt of FDA approval to market the drug (JTX 2133 at 9-10).

clinical development of Tecfidera® to treat MS. Id. at 4-5, 10-11, 14. As Medical Director, Dr. O'Neill proposed that Biogen incorporate a 480mg/day dose of DMF (BID) as part of its Phase II study of Tecfidera® (Dkt. Nos. 358 at 126-27, 362 at 120-21, 125-26, 140; JTX 2013 at 16-17; JTX 2035 at 14; 2133 at 14-16).[7]

Biogen opted instead to test 120mg/day of DMF (in one single dose or "QD"), 360mg/day of DMF (in three equal doses or "TID"), and 720mg/day of DMF (TID) (Dkt. Nos. 358 at 127-28, 135, 362 at 68-70; JTX 2013 at 17; JTX 2036 at 1; JTX 2133 at 16-17) in its Phase II study (JTX 2013 at 17; JTX 2153B at 8, 12). The results of that study, which were published in May 2006, demonstrated that a 720mg/day dose of DMF (TID) was efficacious in treating MS (JTX 2088 at 3-4; JTX 2153B at 8, 12-18), but doses of 120mg/day (QD) and 360mg/day (TID) were not (JTX 2153B at 8, 12-18).

With these results in hand, Biogen began designing its Phase III study (JTX 2091; JTX 2100; JTX 2101; JTX 2133 at 25-26; JTX 2142; JTX). Before that study got underway, however, Dr. O'Neill

[7] Phase II studies are in vivo clinical trials that test a new drug in a mid-sized group of human patients (Dkt. No. 356 at 27 (noting that Biogen's Phase II study included approximately 250 patients)). "In vivo" means inside the body. In other words, an experiment in vivo is done in a living organism (Dkt. No. 358 at 59 (discussing in vivo test performed in mice)).

left the BG-12 program and was replaced by Katherine Dawson, M.D. ("Dr. Dawson") (Dkt. No. 362 at 17, 153-54; JTX 2091 at 1; JTX2133 at 26).

4. Biogen's Research Regarding the Nrf2 Pathway

It must be noted that Biogen's BG-12 Development Program was not focused solely on the clinical development of Tecfidera®. Matvey E. Lukashev, Ph.D. ("Dr. Lukashev"), a scientist employed by Biogen, joined the BG-12 program in 2005 (Dkt. No. 358 at 41; JTX 2196), where his work was to "elucidate the mechanism of action"; he "was not involved in clinical decision-making" (Dkt. No. 358 at 40-41, 42).

"Mechanism of action" is a "scientific fact-based description of the molecular and cellular events affected by the . . . active substance of the drug." Id. at 47. Through his research, Dr. Lukashev discovered that DMF, with its key regulator, a protein called KEAP1, activated the Nrf2 pathway. Id. at 48-49. Based on this mechanism of action, he looked for other compounds that could do the same. Id. at 52.

Dr. Lukashev's scope of work thus extended beyond Biogen's BG-12 testing program because it included screening compounds other than DMF that could activate the Nrf2 pathway. Id. at 52-53. When

asked to describe his work, he noted that it was "a more exploratory nature. It[was] to explore potential for follow-on compound discovery, perhaps movement into other indications or perhaps not previously explored in the clinic in any therapeutic context, combinations of fumarates with other therapeutics." Id. at 53. Significantly, Dr. Lukashev 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. at 53-54, 54.

Although Dr. Lukashev conducted experiments with a range of concentrations of DMF and monomethyl fumarate ("MMF") in vitro and in vivo,[8] those experiments "examine[d] details of the molecular events that could be, in principle, triggered by the active ingredient in a cell." Id. at 54, 57-60. Two of these examples were included in Biogen's U.S. Provisional Application No. 60/888,921 ("the '921 Application") (JTX 2182 at 37-39), and a third was included in Biogen's International Patent Application No.

[8] "In vitro" means outside the body. In other words, an experiment in vitro is an artificial experiment performed using a test tube or petri dish (Dkt. No. 359 at 28 (explaining the meaning of in vitro)).

PCT/US2008/001602 ("the 0016902 Application") (PTX 401 at 33).[9] Dr. Lukashev is the only inventor named in the '921 and 0016902 Applications, entitled "Nrf2 Screening Assays and Related Methods and Compositions," which recite methods for screening drug compounds for their ability to activate the Nrf2 pathway (JTX 2182 at 4, 40-42; PTX 401 at 1-2).

5. Brief Summary of Prosecution History of '514 Patent

Biogen filed the '921 Application on February 8, 2007 (JTX 2182), before beginning its Phase III study of Tecfidera®.[10] It later filed the 0016902 Application, which added to the specification of the '921 Application, on February 7, 2008 (PTX 401). The 0016902 Application later became U.S. Patent Application No. 12/526,296 ("the '296 Application") on August 7, 2009 (DTX 1016).[11]

Biogen received the results of its Phase III study in April 2011, after which it twice amended the '296 Application to change

[9] "PTX" refers to Biogen's trial exhibits.

[10] Phase III studies are in vivo clinical trials that test a new drug in a large number of human patients (Dkt. No. 377 at 16 (noting that Biogen Phase III study involved over 2600 patients (citing JTX 2088; JTX 2133))).

[11] "DTX" refers to Mylan's trial exhibits.

its title and claims and to add an inventor (DTX 1656; DTX 1657). Notably, it did not change the specification in the '296 Application. Id.

Biogen later abandoned the '296 Application in favor of a continuing application, U.S. Patent Application No. 13/326,426 ("the '426 Application"), filed on February 13, 2012 (JTX 2173). Ultimately, the '426 Application resulted in the issuance of the '514 Patent on March 19, 2013 (JTX 2000; JTX 2173). And, it was through its '921 Application that Biogen claimed a February 8, 2007 priority date for its '514 Patent (JTX 2000; JTX 2182).

6. Biogen's Phase III Development of Tecfidera®

After receiving FDA approval for its Phase III study, Biogen commenced its first trial (the DEFINE trial) on March 14, 2007, and its second trial (the CONFIRM trial) on July 28, 2007 (JTX 2108 at 12, 23; JTX 2110 at 28, 38; JTX 2133 at 27-28). Although the parties dispute when and why Biogen decided to test a 480mg/day dose of DMF as part of those trials (Dkt. Nos. 376 at 11-12, 377 at 14-15), it is undisputed that, for whatever reason it did so, Biogen ultimately included a 480mg/day dose of DMF (BID) as part of its Phase III study.

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The Phase III study "showed an unexpected magnitude of efficacy where the 480mg/day dose 'met all primary and secondary endpoints' including both MRI and clinical endpoints, e.g., reduction in annual relapse rate, and did so 'with a high level of statistical significance'" (Dkt. No. 377 at 17 (emphasis omitted) (quoting JTX 2088 at 9-10, 19)). Put simply, the Phase III study demonstrated that the 480mg/day and 720mg/day doses of DMF were equally efficacious in treating MS.

7. Biogen's Prosecution of the '514 Patent

In light of these unexpected results, Biogen needed a patent to protect the 480mg/day dose from competition and quickly filed U.S. Provisional Application No. 14/119,373 ("the '373 Application") in May 2011. This application was entitled "Methods of Treating Multiple Sclerosis and Preserving and/or Increasing Myelin Content" and listed three inventors, Dr. Dawson, Dr. O'Neill, and Alfred Sandrock (another Biogen employee) (DTX 1169). The specification of the '373 Application thoroughly reviewed data from Biogen's Phase III study and asserted 42 claims reciting a method for treating MS with a 480mg/day dose of DMF (BID). Id.

A month after filing the '373 Application, in June 2011, Biogen amended its '296 Application, filed on August 7, 2009, to

replace the title "Nrf2 Screening Assays and Related Methods and Compositions" with "Treatment for Multiple Sclerosis" (DTX 1656). This amendment also deleted all previously listed claims for methods for screening drug compounds for their ability to activate the Nrf2 pathway and added sixteen new claims reciting methods for treating MS with a 480mg/day dose of DMF (BID). Id. In October 2011, Biogen again amended the '296 Application, this time to add Dr. O'Neill as a co-inventor with Dr. Lukashev and also to include three additional claims reciting methods for treating MS with 480mg/day of DMF (BID) (DTX 1657).

At no time throughout this course of amendments did Biogen amend the "specification" (i.e., the written description) of the '296 Application (DTX 1656; DTX 1657). This enabled it to claim a priority date of February 8, 2007, the date on which Biogen had filed the '921 Application (JTX 2182).[12]

[12] See Auto. Tech Int'l, Inc. v. Delphi Corp., 776 F. Supp. 2d 469, 488 (E.D. Mich. 2011) ("[A] patent containing enabled and adequately described claims that issue from a continuation application may claim the benefit of the priority date of its parent application because they share identical specifications; a continuation application may not contain new matter." (citing 35 U.S.C. § 120)). The parties, however, dispute whether Biogen may rely on example three (Dkt. Nos. 376 at 22 n.6, 377 at 25 n.4, 384 at 11-12), which was included only in the 0016902 Application (PTX 401 at 33), not Biogen's earlier '921 Application (JTX 2182 at 37-39). This dispute is discussed in detail infra in Part III

Later, on February 13, 2012, Biogen filed a continuing application of its '296 Application, which ultimately became the '426 Application (JTX 2173). The '426 Application included all amendments to the '296 Application, while maintaining the specification from the '921 Application. Id. Biogen then abandoned the '296 Application and focused its efforts before the U.S. Patent and Trademark Office ("PTO") entirely on the '426 Application. Id.

During prosecution of the '426 Application, the PTO twice rejected Biogen's asserted claims as obvious over the prior art (JTX 2173 at 382-92, 888-96). In response to each rejection, Biogen reasserted its claim that the 480mg/day dose of DMF (BID) had exhibited unexpected efficacy in the treatment of MS. Id. at 453-55, 914-17.

The PTO eventually overcame its concerns about obviousness and, on March 19, 2013, issued the '514 Patent (JTX 2000), which is listed in the Orange Book for NDA No. 204063, covering Tecfidera® (Dkt. No. 1 at 15), and claims a priority date of February 8, 2007

(Discussion).

(JTX 2000). With the '514 Patent in hand, Biogen abandoned the '373 Application it had filed on May 26, 2011 (DTX 1169).[13]

8. The Asserted Claims of the '514 Patent

The asserted claims in the '514 Patent recite a method for treating a specific disease (MS), with a specific drug (DMF or MMF), at a specific dose (480mg/day (BID)) (Dkt. No. 359 at 89-90, 105):

> 1. 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 [DMF], [MMF], or a combination thereof, and (b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of [DMF], [MMF], or a combination thereof is about 480 mg per day.
>
> 2. The method of claim 1, wherein the pharmaceutical composition is administered in the form of a tablet, a suspension, or a capsule.
>
> 3. The method of claim 1, wherein the therapeutically effective amount is administered in separate administrations of 2, 3, 4, or 6 equal doses.

[13] An addendum attached to this Memorandum Opinion and Order provides a timeline of this prosecution history.

4. The method of claim 3, wherein the therapeutically effective amount is administered in separate administrations of 2 equal doses.

. . .

6. The method of claim 1, wherein the pharmaceutical composition consists essentially of [DMF] and one or more pharmaceutically acceptable excipients.

. . .

8. The method of claim 1, wherein the pharmaceutical composition is administered to the subject for at least 12 weeks.

9. The method of claim 6, wherein the therapeutically effective amount is administered to the subject in 2 equal doses.

10. The method of claim 9, wherein the therapeutically effective amount is administered to the subject for at least 12 weeks.

11. A method of treating a subject in need of treatment for multiple sclerosis consisting essentially of orally administering to the subject about 480 mg per day of [DMF], [MMF], or a combination thereof.

12. The method of claim 11, wherein about 480 mg of [DMF] per day is administered to the subject.

> 13. The method of claim 12, wherein the [DMF] is administered in separate administrations of 2 equal doses.
>
> . . .
>
> 15. A method of treating a subject in need of treatment for multiple sclerosis comprising orally administering to the subject pharmaceutical composition consisting essentially of (a) a therapeutically effective amount of [DMF] and (b) one or more pharmaceutically acceptable excipients, wherein the therapeutically effective amount of [DMF] is about 480 mg per day.
>
> 16. The method of claim 15, wherein the [DMF] is administered in separate administrations of 2 equal doses.

(JTX 2000 at 28-29).

III. DISCUSSION

A. Applicable Law

The first paragraph of 35 U.S.C. § 112 requires a patent's specification to include, among other things, "a written description of the invention . . . ."[14] This written description

[14] The America Invents Act ("AIA"), Pub. L. No. 112-29, § 4(c), 125 Stat. 284, 296 (2011), added subsection headings to the six paragraphs that made up the pre-AIA version of § 112. Although these amendments have no effect on the question presented, the parties agree that, because the priority date of the '514 Patent is February 8, 2007, the pre-AIA version of § 112 applies to the asserted claims (Dkt. Nos. 376 at 17 n.3, 377 at 21 n. 3).

requirement "allows a person of skill in the art to recognize that the patentee invented what is claimed." Synthes USA, LLC v. Spinal Kinetics, Inc., 734 F.3d 1332, 1341 (Fed. Cir. 2013) (citing Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc)). "[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor ha[d] possession of the claimed subject matter as of the filing date." Id. (quoting same).

"That requirement is satisfied only if the inventor 'conveys 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 demonstrates that by disclosure in the specification of the patent.'" Nuvo Pharm. (Ir.) Designated Activity Co. v. Dr. Reddy's Labs. Inc., 923 F.3d 1368, 1376 (Fed. Cir. 2019) (cleaned up) (quoting Centocor Ortho Biotech, Inc. v. Abbott Labs., 636 F.3d 1341, 1348 (Fed. Cir. 2011)). "[A]ctual 'possession' or reduction to practice outside of the specification is not enough." Ariad Pharm. Inc., 598 F.3d at 1352. "[I]t is the specification itself that must demonstrate possession." Id.

Whether the '514 Patent is invalid for lack of written description is a factual question for Mylan to establish by clear

and convincing evidence. Rivera v. Int'l Trade Comm'n, 857 F.3d 1315, 1319 (Fed. Cir. 2017).

B. Person of Ordinary Skill in the Art

Determining who constitutes a person of ordinary skill in the art ("POSA") is also a factual question, see ALZA Corp. v. Andrx Pharm., LLC, 603 F.3d 935, 940 (Fed. Cir. 2010), involving a two-step inquiry: "The first part is determining what exactly is that 'relevant art' at issue, the second is determining who qualifies as a 'person of ordinary skill' in that art." Seed Research Equip. Solutions, LLC v. Gary W. Clem, Inc., No. 09-01282-EFM-KGG, 2011 WL 5024351, at *3 (D. Kan. Oct. 20, 2011) (citing Arachnid, Inc. v. Merit Indus., Inc., 201 F. Supp. 2d 883, 888 (N.D. Ill. 2002)).

"Art" is defined simply as "[a] field of useful endeavor." And "relevant art" is the "[a]rt to which one can reasonably be expected to look for a solution to the problem that a patented device tries to solve." Art, Black's Law Dictionary (11th ed. 2019). "The relevant art is defined by the nature of the problem confronting the would-be inventor." Ryko Mfg. Co. v. Nu-Star, Inc., 950 F.2d 714, 716 (Fed. Cir. 1991) (internal quotation omitted). "Factors that may be considered in determining level of ordinary

skill in the art include: (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." Daiichi Sankyo Co., Ltd. v. Apotex, Inc., 501 F.3d 1254, 1256 (Fed. Cir. 2007) (citation omitted). These factors are illustrations, not exhaustive. Id.

In this case, the parties agree that a 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" (Dkt. Nos. 356 at 113; 359 at 9, 81; 387 at 1). Mylan presented the testimony of Benjamin M. Greenberg, M.D. ("Dr. Greenberg"), and Biogen presented the testimony of Daniel R. Wynn, M.D. ("Dr. Wynn") (Dkt. Nos. 356 at 99-228, 359 at 6-73, 74-144). Each is a neurologist who treats patients with MS and meets the parties' definition of a POSA (Dkt. Nos. 356 at 165-66, 359 at 80).

C. The Parties' Contentions

Mylan contends that the '514 Patent is invalid for lack of written description because the specification described in 2007

bears no resemblance to the invention claimed in 2011 (Dkt. No. 376 at 16-17). This is so for two reasons. First, as Biogen insisted throughout its prosecution of the '514 Patent, a POSA would not have expected the claimed invention——a 480mg/day dose of DMF (BID)——to effectively treat MS. Id. at 17-24. Mylan asserts that nothing in the specification of the '514 Patent teaches otherwise. Id.

Second, Mylan contends that, when viewed as an integrated whole, the combination of selectively-plucked disclosures in the specification of the '514 Patent fails to sufficiently describe the claimed invention——a method of treating MS with a therapeutically effective amount of DMF, i.e., 480mg/day of DMF (BID). Id. at 24-29. According to Mylan, "[t]he reason is evident: Biogen grafted the '514 claims onto a specification written to cover an entirely different set of inventions, conceived of by an entirely different inventor, and filed more than four years before Biogen's 2011 Phase III trial results demonstrated the effectiveness of the 480[mg/day] dose." Id. at 24 (emphasis in original).

In resisting these arguments, Biogen asserts that Mylan faces an "added burden" of demonstrating lack of written description in this case because the PTO previously questioned the sufficiency of

the written description in the context of an obviousness rejection (Dkt. No. 377 at 20-21). It also contends that Mylan mistakenly relies on evidence of obviousness, which is irrelevant to the written-description analysis. Id. at 22. Turning to the specification, Biogen maintains that "[t]he '514 Patent links through Method 4 each of the three recited elements of the asserted claims: (1) a method of treating MS with (2) DMF and/or MMF (3) at a dose of 480 mg per day." Id. at 23, 23-29. Finally, Biogen argues that Mylan has misapplied the law and failed to satisfy its burden of proof. Id. at 29-45. The Court addresses each of these arguments in turn.

D. The Asserted Claims of the '514 Patent Are Invalid for Lack of Written Description Under § 112

1. Mylan Faces No "Added Burden"

As a threshold matter, Biogen's argument that Mylan faces an "added burden" in this case misses the mark. As Mylan correctly notes, "[t]he burden [of proof] does not suddenly change to something higher—'extremely clear and convincing evidence' or 'crystal clear and convincing evidence'— simply because" the PTO previously questioned the sufficiency of the written description in the context of an obviousness rejection. In Sciele Pharma Inc. v.

Lupin Ltd., 684 F.3d 1253, 1260 (Fed. Cir. 2012), the Federal Circuit confirmed the applicable burden of proof for establishing invalidity based on obviousness: "The presumption of validity found in [35 U.S.C.] § 282 is reflected in the standard of proof required to prove invalidity, clear and convincing evidence." Id. (citing Microsoft Corp. v. i4i Ltd. P'ship, 564 U.S. 91, 100-01 (2011)). So too here. "Nothing in § 282's text suggests that Congress meant to . . . enact a standard of proof that would rise and fall with the facts of each case." Microsoft Corp., 564 U.S. at 109.

2. The Specification Does Not Demonstrate that the Inventors "Possessed" the Claimed Invention

In order to satisfy the written description requirement of § 112, the inventor must "'convey[] 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[] that by disclosure in the specification of the patent.'" Nuvo Pharm., 923 F.3d at 1376 (cleaned up) (citation omitted). Significantly, "actual 'possession' or reduction to practice outside of the specification is not enough." Ariad Pharm. Inc., 598 F.3d at 1352. "[I]t is the specification itself that must demonstrate possession." Id.

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Here, Mylan contends that the '514 Patent, when viewed as an integrated whole, fails to satisfy this statutory requirement because it does not demonstrate that, as of February 8, 2007, Dr. Lukashev and Dr. O'Neill "possessed" a method of treating MS with a therapeutically effective amount of DMF, i.e., 480mg/day (BID) (Dkt. Nos. 376, 384).[15]

Spanning 30 columns (JTX 2000 at 15-29), the specification of the '514 Patent begins with a general discussion of MS but quickly turns to a discussion of how "the Nrf2 pathway may be activated in neurodegenerative and neuroinflammatory diseases as an endogenous protective mechanism," and how "[e]merging evidence suggests that [plant-derived] compounds may exert their neuroprotective effects by activating cellular stress-response pathways, including the Nrf2 pathway, resulting in the upregulation of neuroprotective genes"

[15] In its post-trial brief, Biogen appears to suggest that the therapeutic efficacy required by the asserted claims differs from clinical efficacy (Dkt. No. 377 at 39-40). But based on the factual and evidentiary record in this case, and in light of Biogen's consistent representations to the PTO during prosecution and before the PTAB in the related IPR proceeding, Biogen is estopped from relying on this distinction. See, e.g., New Hampshire v. Maine, 532 U.S. 742, 743 (judicial estoppel applies "to protect the integrity of the judicial process by prohibiting parties from deliberately changing positions according to the exigencies of the moment" (cleaned up)).

(JTX 2000 at 15). It then acknowledges that "the exact mechanism of action of these compounds remains poorly understood." Id.

The specification provides five methods:

> 1) methods of screening for at least one new candidate compound for treating a neurological disease;
>
> 2) methods of evaluating neuroprotective properties of at least one drug candidate for treating a neurological disease;
>
> 3) methods of comparing (e.g., for bioequivalence) at least two pharmaceutical compositions which comprise fumaric acid derivatives;
>
> 4) methods of treating a neurological disease by administering to the subject in need thereof at least one compound that is partially structurally similar to DMF or MMF; and
>
> 5) methods of treating a neurological disease by a combination therapy that comprises administration of at least one first compound that upregulates the Nrf2 pathway and at least one second compound that does not upregulate the Nrf2 pathway.

Id. at 15-16.

Biogen concedes that "Methods 1-3 are directed to methods of screening for compounds to treat neurological diseases," which are "described, but not claimed, in the '514 Patent" (Dkt. No. 377 at 16, 24). It also concedes that "Method 5 relates to the use of

[compounds such as DMF] in combination therapy along with other compounds having different activity." Id. at 24. According to Biogen, "[t]he '514 Patent links through Method 4 each of the three recited elements of the asserted claims: (1) a method of treating MS with (2) DMF and/or MMF (3) at a dose of 480 mg per day." Id. at 23. This simply is not so. The description of Method 4 is limited in scope and makes no mention of treating MS with a 480mg/day dose of DMF (BID):

> In some embodiments method 4 comprises administering to the mammal a therapeutically effective amount of at least one neuroprotective compound having Formula I, II, III, or IV, e.g., a fumaric acid derivative (e.g. , DMF or MMF).
>
> In some embodiments method 4 provides a method of slowing or preventing neurodegeneration in a patient in need thereof, by administering the compound in an amount and for a period of time sufficient to slow or prevent demyelination, axonal loss, and/or neuronal death, e.g., by at least 30% relative to a control.

(JTX 2000 at 16).

> Also provided are 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 MMF.
>
> In some embodiments of method 4, a method of treating a mammal who has or is at risk for

> a neurological disease is provided. The methods comprises [sic] administering to the mammal a therapeutically effective amount of at least one neuroprotective compound which has Formula I, II, III, or IV, e.g., a fumaric acid derivative (e.g., DMF or MMF).
>
> In some embodiments of method 4, a method of slowing or preventing neurodegeneration (more specifically, e.g., demyelination, axonal loss, and/or neuronal death) in a subject in need thereof by administering the at least one compound in an amount and for a period of time sufficient to do at least one of slow or prevent demyelination, slow or prevent axonal loss, and slow or prevent neuronal death, e.g., by at least 30%, 50%, 100% or higher over a control over a period of at least 5, 10, 12, 20, 40, 52, 100, or 200 weeks, or more.

Id. at 18.

Thus, 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." Novozymes A/S v. DuPont Nutrition Biosciences APS, 723 F.3d 1336, 1349 (Fed. Cir. 2013). Indeed, in Column 3, the specification explains that, "[i]n some embodiments, the neurological disease is a neurodegenerative disease such as, for example, ALS, Parkinson's disease, Alzheimer's disease, and Huntington's disease" (JTX 2000 at 16). In others, "the neurological disease is MS or another demyelinating neurological disease." Id.

Column 16 then provides an exhaustive list of "diseases suitable for the [five] methods described" in the '514 Patent:

> Examples of neurological diseases suitable for the methods described herein include neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS), Parkinson's disease, Alzheimer's disease, and Huntington's disease. Other examples include demyelinating neurological disease including, in addition to MS, the following diseases: acute haemorrhagic Ieucoencephalomyelitis, Hurst's disease, acute disseminated encephalomyelitis, optic neuritis, Devic's disease, spinal cord lesions, acute necrotizing myelitis, transverse myelitis, chronic progressive myelopathy, progressive multifocal leukoencephalopathy (PML), radiation myelopathy, HTLV-1 associated myelopathy, monophasic isolated demyelination, central pontine myclinolysis, and leucodystrophy (e.g., adrenoleucodystrophy, metachromatic leucodystrophy, Krabbe's disease, Canavan's disease, Alexander's disease, Pelizaeus-Merbacher disease, vanishing white matter disease, oculodentodigital syndrome, Zellweger's syndrome), chronic inflammatory demyelinating polyneuropathy (CIDP), acute inflammatory demyelinating polyneuropathy (AIDP), Leber's optic atrophy, and Charcot-Marie-Tooth disease.
>
> Additional examples of diseases suitable for the methods described herein include polyneuritis and mitochondrial disorders with demyelination. These disorders may be co-presented with, and possibly aggravated by diabetes, e.g., insulin-dependent diabetes mellitus (IDDM; type I diabetes), or other diseases.

Id. at 22.

Because Methods 1-5 can be used for a plethora of neurological diseases, there are no "blaze marks" in Method 4 that would lead a POSA specifically to MS. Ariad, 598 F.3d at 1348. Nor, as Biogen posits, does Method 4 "link" a therapeutically effective amount of DMF to a dose of 480mg/day (BID). Id. at 1357.

For this proposition, Biogen directs the Court's attention to Column 18, the only part of the specification that mentions 480mg/day of DMF:

> For example, an effective dose of DMF or MMR to be administered to a subject orally can be from about 0.1 g to 1 g per pay [sic], 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.[16]

(JTX 2000 at 23) (footnote added). This passage, however, neither "links" this "effective dose" to the treatment of MS, nor to a 480mg/day dose of DMF (BID). Mylan's POSA, Dr. Greenberg, credibly testified at trial that nothing in Column 18 ties an effective dose of DMF specifically to the treatment of MS (Dkt. No. 359 at 34-36).

[16] Although this passage reads "an effective dose of DMF or MMR," the parties agree that "MMR" is a typographical error and should read "MMF" (Dkt. Nos. 356 at 90, 358 at 73, 362 at 40).

The cited passage, moreover, offers only a broad range of what an effective dose "can be": "0.1 g to 1 g per day"[17] or "200 mg to 800 mg per day" (JTX 2000 at 23).

The examples following this broad disclosure also fail to direct a POSA to the conclusion that a therapeutically effective amount of DMF is 480mg/day (BID). Strikingly, 480mg dosing is mentioned only once in three examples: "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" (JTX 2000 at 23 (emphasis added)). Although Biogen and its expert insist that 480mg to 720mg/day is the narrowest and, therefore, the most preferred range, thereby teaching a 480mg/day dose (Dkt. Nos. 359 at 49-50, 102, 143-44; 377 at 27, 29), this reading is neither credible nor persuasive.

Based on the results of Biogen's Phase II study, as of the claimed priority date of February 8, 2007, a POSA would have known that 720mg/day of DMF (TID) is a therapeutically effective dose for treating MS, and that lower doses, such as 360mg/day of DMF (TID) and 120mg/day of DMF (QD), are not (JTX 2153B at 8, 12). See Zoltek Corp. v. United States, 815 F.3d 1302, 1308 (Fed. Cir. 2016) (stating that the written-description "requirement is applied in

[17] In other words, 100mg to 1,000mg (Dkt. No. 359 at 34).

the context of the state of knowledge at the time of the invention" (citation omitted)). Thus, on reading the specification, a POSA would be drawn to, if anything, the 720mg/day dose of DMF included in each dosing example: "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" (JTX 2000 at 23 (emphasis added)). This understanding is confirmed by the next sentence, which further highlights a 720mg/day dose: "For example, the 720 mg per day may be administered in separate administrations of 2, 3, 4, or 6 equal doses." Id. (emphasis added).

Given the emphasis on 720mg/day of DMF, nothing in this passage teaches a POSA that a 480mg/day dose of DMF (BID) is therapeutically effective for treating MS (Dkt. No. 359 at 34-38). Tellingly, Biogen's expert, Dr. Wynn, conceded as much on cross examination. Based on his reading of the '514 Patent, he testified he would not know which dose provided in Column 18 would be most effective for treating MS:

> Q. So based upon reading the patent alone, you wouldn't know what the preferred dose was for treating MS? Is that what I just heard you say?
>
> A. Which would be the most effective dose.
>
> Q. Okay. You wouldn't know that?

A. Correct.

. . .

Q. Based on the data the artisan would know at the time of the filing of the patent, all three of those ranges include doses which, according to you, they would know would be ineffective, right?

A. A dose of 360 or lower would not be felt to be a preferred dose for treating MS.

Q. Okay. So -- but we get to the fourth dose, and suddenly now we're talking about treating MS, right?

A. I don't know that the others were not for treating MS. And, again, from reading this, I don't know that 480 would be the preferred dose for treating MS either.

Q. And that's -- I think we agree on that. Reading this patent specification as a person of skill in the art, you wouldn't know that 480 milligrams would be a preferred dose for treating MS. I agreed with you on that, right? We agree on that?

A. Okay.

(Dkt. No. 359 at 135-37).

After Dr. Wynn attempted to disavow this testimony, id. at 137-38, Mylan effectively impeached his credibility:

Q. All right, Doctor. I'm looking at the Delaware trial transcript at page 64, lines 13 to 18. Do you see that?

. . .

> A. Yes.
>
> Q. And do you see you were asked a question there, "Actually, sir, if you had seen this patent in 2007, you wouldn't know about the 480 milligram dose, would you?" And what was your answer?
>
> A. I answered, "I wouldn't know if it was clinically effective."
>
> Q. And then you were asked, "Because there's no data on it provided in the specification, right?" And what did you answer?
>
> A. "Anywhere that I'm aware of."
>
> Q. All right. That was the testimony you gave in Delaware, correct, sir?
>
> A. Yes.

Id. at 139.

Biogen's reliance on Example 3 fares no better. To start, Biogen may not rely on this example because it was not in the specification of the '921 Application (JTX 2182 at 37-39) through which the '514 Patent claims priority (JTX 2000). See Delphi Corp., 776 F. Supp. 2d at 488 (noting that "a continuation application may not contain new matter" (citing 35 U.S.C. § 120)). Even had it been included in the '921 Application, Example 3 plainly does not teach a therapeutically effective amount of DMF for treating MS in humans (JTX 2000 at 24-25).

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Although it employs Experimental Autoimmune Encephalomyelitis ("EAE"), the animal model of MS, not even Dr. O'Neill, who is a POSA himself and named inventor of the '514 Patent, could explain the relevance of Example 3——or any of the examples in the '514 Patent——to the claimed invention. Id. The same holds true of Dr. Wynn. On direct examination, he merely testified that Example 3 is a study of DMF and MMF in conjunction with EAE, an animal model of MS (Dkt. No. 359 at 95, 98). He never explained how that experiment teaches a method of treating MS (in humans, not mice) with a therapeutically effective amount of DMF, i.e., 480 mg/day (BID). Id.

One need only recall Dr. Lukashev's trial testimony to discern the reason for this omission. Dr. Lukashev credibly testified that the three examples in the '514 Patent were part of his research, which "was separate from preclinical development" and unrelated to the clinical application of DMF (Dkt. No. 358 at 60-61).[18] The examples had "nothing to do with the efficacy [of DMF] in clinical disease" and would not be "helpful in identifying a therapeutically effective amount of [DMF]." Id. at 61. Indeed, the results of

[18] Dr. Lukashev, while not a POSA, is a named inventor who supplied the information in the specification (Dkt. No. 358 at 57). Ignoring his credible testimony would be unreasonable.

Example 3 "provide[d] evidence of [MMF] and [DMF] activation of NRF2 in vivo." Id. at 59-60, 60. Mylan's POSA, Dr. Greenberg, concurred with Dr. Lukashev's testimony (Dkt. No. 359 at 70).

The disparity between the '514 Patent's specification and the claimed invention of the '921 and the 0016902 Applications (JTX 2182; PTX 401) is not surprising given the stark differences between Dr. Lukashev and Dr. O'Neill's respective roles in the BG-12 Development Program. From the evidence presented at trial, Dr. Lukashev's research regarding the activation of the Nrf2 pathway and screening drug compounds had nothing to do with the clinical development of Tecfidera® (Dkt. No. 358 at 60-61). That task fell to Dr. O'Neill and later Dr. Dawson (Dkt. No. 362 at 17, 153-54; JTX 2091 at 1; JTX2133 at 26). Notably, Dr. O'Neill's hypothesis, that a 480mg/day dose of DMF (BID) would be efficacious in treating MS, evolved from his review of Fumapharm's confidential studies of Fumaderm® (Dkt. No. 362 at 27-28, 52-54), not Dr. Lukashev's unrelated research regarding the mechanism of action.

In sum, Biogen has attempted to satisfy the written description requirement of § 112 by selectively plucking specific words from the specification that correspond to each element of the claimed invention. The United States Court of Appeals for the

Federal Circuit has squarely rejected this approach. Nuvo Pharm., 923 F.3d at 1380 ("We have expressly rejected the 'argument that the written description requirement . . . is necessarily met as a matter of law because the claim language appears in ipsis verbis in the specification.'" (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 968 (Fed. Cir. 2002))).[19] The '514 Patent thus must be viewed as an integrated whole rather than a sum of its parts. Novozymes A/S, 723 F.3d at 1349 ("Taking each claim . . . as an integrated whole rather than as a collection of independent limitations . . . .").

With no support in the text of the specification, Biogen must rely on Dr. O'Neill's repeated insistence that he invented the 480mg/day dose of DMF (BID) to treat MS (Dkt. No. 362 at 17-111). But "inventor testimony cannot establish written description support where none exists in the four corners of the specification . . . ." Nuvo Pharm., 923 F.3d at 1381. Put simply, Dr. O'Neill's testimony offers no more than "actual possession," which is insufficient to satisfy § 112. Ariad, 598 F.3d at 1352 ("[A]ctual

[19] In other words, written description is not satisfied simply because the same words appear in the claims and the specification. See *Ipsissima verba*, Black's Law Dictionary (11th ed. 2019) (meaning "the very (same) words").

'possession' . . . is not enough."). "There must be some description, such as a constructive reduction to practice, establishing that the inventor 'was in possession of the . . . claimed invention, including all of the elements and limitations.'" Nuvo Pharm., 923 F.3d at 1380-81 (quoting Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 926 (Fed. Cir. 2004)).

"The essence of th[is] written description requirement is that a patent applicant, as part of the bargain with the public, must describe his or her invention so that the public will know what it is and that he or she has truly made the claimed invention." AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc., 759 F.3d 1285, 1298 (Fed. Cir. 2014). "Patents are not rewarded for mere searches, but are intended to compensate their successful completion." Nuvo Pharm., 923 F.3d at 1381 (citing Ariad, 598 F.3d at 1353). "That is why the written description requirement incentivizes actual invention, and thus a mere wish or plan for obtaining the claimed invention is not adequate written description." Id. (cleaned up) (citations omitted).

Because the text of the specification in the '514 Patent does not demonstrate that, as of February 8, 2007, Dr. Lukashev and Dr. O'Neill "possessed" the claimed invention——a method of treating MS

with a therapeutically effective amount of DMF, i.e., 480mg/day (BID)——Biogen has failed to satisfy its part of the bargain.

3. Extrinsic Evidence Confirms the Lack of Written Description

If the text were not enough, extrinsic evidence further "illuminates the absence of critical description . . . ." Nuvo Pharm., 923 F.3d at 1381. In this case, that evidence is substantial.

Turning first to the specification of the '373 Application, it is undisputed that Biogen filed this application one month after receiving the "unexpected" results of its Phase III study establishing the efficacy of a 480mg/day dose of DMF (BID) to treat MS (DTX 1169). Entitled "Methods of Treating Multiple Sclerosis and Preserving and/or Increasing Myelin Content," the application claimed methods for treating MS with a 480mg/day dose of DMF (BID), and listed Dr. Dawson, Dr. O'Neill, and Alfred Sandrock as inventors. Id. As one would expect, the specification provided and discussed in detail a wealth of data generated during Biogen's Phase III study. Id. In contrast, the specification in the '514 Patent included none of this data or information (compare DTX 1169 with JTX 2000).

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The explanation for this omission is readily apparent from the record. Despite Dr. O'Neill's strong belief that a 480mg/day dose of DMF (BID) would effectively treat MS (Dkt. No. 362 at 61 ("I had this strong belief and hypothesis that 480 milligrams could work in the treatment of MS.")), Biogen did not know that to be true until its receipt of the "unexpected" results of its Phase III study (JTX 2088 at 9-10, 19). Moreover, upon recognizing that it had no patent to protect a 480mg/day dose of DMF (BID) from competition, Biogen quickly filed the '373 Application with a priority date of May 26, 2011 (DTX 1169). Problematically, that application likely would not have protected the 480mg/day dose of DMF (BID) from § 112 invalidity challenges based on the prior art before May 26, 2011. Id.

In an attempt to resolve this problem, Biogen amended its '296 Application, sitting idle since August 7, 2009 (DTX 1016), which stemmed from the earlier '921 and 0016902 Applications (JTX 2182; PTX 401). It deleted the original title and claims of the '296 Application, added a new title, new claims, and a new inventor (DTX 1656; DTX 1657). But it left the specification unchanged in an

effort to obtain the '921 Application's priority date of February 8, 2007, and avoid over four years of prior art.[20]

This strategy came with a cost, however, since Biogen was left with a specification written in 2007 that bore no resemblance to the '514 Patent's title and claimed invention——a method of treating MS with a therapeutically effective amount of DMF, i.e., 480mg/day (BID) (compare DTX 1169 with JTX 2000)——an invention that no one knew would work until April 2011 when Biogen received the results of its Phase III study (JTX 2088 at 9-10, 19). Dr. O'Neill's testimony supports this conclusion: "I believed from the outset that 480 milligrams as two divided doses of 240 milligrams a day would demonstrate efficacy. I was very pleased when we saw the Phase 3 results to see that 480 milligrams was efficacious and actually had a high degree of efficacy" (Dkt. No. 362 at 60). Consequently, "there is nothing in the specification of the patent[]-in-suit showing 'that the inventor[s] actually invented the invention claimed.'" Nuvo Pharm., 923 F.3d at 1380 (emphasis omitted) (quoting Centocor Orth Biotech Inc., 636 F.3d at 1348).

[20] To underscore this strategy's importance, one need look no further than the PTAB's decision in the parties' related IPR proceeding, where Biogen successfully defeated Mylan's invalidity challenge based on obviousness over prior art. Mylan Pharm. Inc., 2020 WL 582736.

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The Court is well aware that the Federal Circuit "does not require experimental data demonstrating effectiveness." Id. (citation omitted). Nor does it "require theory or explanation of how or why a claimed composition will be effective." Id. (citation omitted). But "the lack of any disclosure of examples may be considered when determining whether the claimed invention is adequately described." Boston Scientific Corp. v. Johnson & Johnson, 647 F.3d 1353, 1364 (Fed. Cir. 2011).

Here, the disparities between the specifications——including related examples——of the '373 Application and the '514 Patent are stark (compare DTX 1169 with JTX 2000). And because a POSA would not have expected a 480mg/day dose of DMF (BID) to be efficacious in 2007 (in fact, according to Biogen's own employee and expert testimony, the efficacy of the 480mg/day dose of DMF (BID) was "unexpected" four years later in April 2011 (Dkt. Nos. 359 at 115 (Dr. Wynn agreeing with Dr. Dawson's declaration)), the '514 Patent's omissions in this regard are particularly telling. To start, the '514 Patent does not include examples discussing efficacy data regarding relapse and disability, lesion loads, quality of life, preserving/increasing myelin content, or clinical trials, all of which was included in Biogen's abandoned '373

Application (compare DTX 1169 at 28-29 with JTX 2000). There are no graphs or data regarding proportion of relapses, distribution of relapses, risk of relapse, progression of disability, distribution of new or newly enlarging lesions, change in baseline, annualized relapse rate, MRI results, lesion volume, or brain atrophy (compare DTX 1169 at 2-19 with JTX 2000). Nor are there summaries, brief or detailed, of the claimed invention (compare DTX 1169 at 20-28 with JTX 2000).

Further, the '514 Patent does not include any Phase I data from the BG-12 Development Program or the confidential data reviewed by Dr. O'Neill during the Fumapharm due diligence (Dkt. No. 362 at 52-55 (discussing what Fumapharm data consisted of); JTX 2000). Nor does it include information about the "C_{max} of DMF," on which he based his entire hypothesis (Dkt. No. 362 at 53-54 ("I believed and I hypothesized was that the -- a frequency of twice a day of a Cmax could be driving efficacy. . . . That is a Cmax of DMF.)).

This case bears a striking resemblance to Nuvo Pharmaceuticals, where the Federal Circuit considered whether the patents-in-suit adequately described the claimed effectiveness of uncoated proton pump inhibitors ("PPIs"). 923 F.3d at 1372, 1376.

The generic defendants had argued that the written description was insufficient because a POSA "would not have expected uncoated PPIs to be effective, and nothing in the specification would teach a [POSA] otherwise." Id. at 1377. The Federal Circuit agreed:

> In light of the fact that the specification provides nothing more than the mere claim that uncoated PPI might work, even though [POSAs] would not have thought it would work, the specification is fatally flawed. It does not demonstrate that the inventor possessed more than a mere wish or hope that uncoated PPI would work, and thus it does not demonstrate that he actually invented what he claimed . . . .

Id. at 1381.

So too here. At every stage of this case and the related IPR proceeding, Biogen defended against Mylan's obviousness challenge by insisting that a POSA would not have expected a 480mg/day dose of DMF to be efficacious in treating MS (Dkt. No. 356 at 56 (Biogen's opening statement: "Dr. O'Neill's claimed invention of using 480 milligrams per day of DMF to treat MS exhibited an unexpected magnitude of efficacy rendering the claimed method nonobvious on this basis alone." (emphasis added))). See also Mylan Pharm. Inc., 2020 WL 582736, at *16 (stating that Biogen "provides argument and evidence . . . that the 480 mg/day dose had an unexpected magnitude of efficacy as compared to a much higher 720

mg/day dose" (emphasis added)). This statement only underscores the failure of the specification to teach a POSA, who would expect otherwise, that a 480mg/day dose of DMF (BID) is efficacious in treating MS. See Nuvo Pharm., 923 F.3d at 1381.

Biogen cannot successfully distinguish Nuvo from the case at hand (Dkt. No. 377 at 34-41). In Nuvo, the specification of the patents-in-suit explicitly acknowledged that a POSA would not have expected uncoated PPIs to work. Id. (discussing Nuvo). Because there is no such acknowledgment in the '514 Patent's specification, Biogen contends that Nuvo's holding is inapposite. Id. This is a distinction without a difference, however. Although the specification at issue in Nuvo explicitly acknowledged what a POSA would not have expected to work, it is well established (as Biogen's own brief acknowledges (Dkt. No. 377 at 33-34)) that a specification "need not include information that is already known and available to the experienced public." Space Sys./Loral, Inc. v. Lockheed Martin Corp., 405 F.3d 985, 987 (Fed. Cir. 2005) (citation omitted). Thus, the specification of the '514 Patent need not explicitly acknowledge that the experienced public (i.e., a POSA) would not have expected a 480mg/dose of DMF (BID) to be efficacious in treating MS.

IV. CONCLUSION

Mylan has established by clear and convincing evidence that the asserted claims of the '514 Patent are invalid for lack of written description. First, the text of the specification does not reasonably convey to a POSA that Dr. Lukashev and Dr. O'Neill "actually invented" a method of treating MS with a therapeutically effective amount of DMF, i.e., 480mg/day BID, as of February 8, 2007. This reading of the text is confirmed by the testimony of Dr. Greenberg, Dr. Lukashev, Dr. O'Neill, and Dr. Wynn. Second, the context of the '514 Patent's prosecution history and the significant omissions from the specification further underscore the failure to adequately describe the claimed invention. Biogen's attempt to avoid this conclusion by combining a few selectively-plucked disclosures from the specification of the '514 Patent has been squarely rejected by the Federal Circuit.

Therefore, for the reasons discussed, the Court **FINDS** that Mylan has satisfied its burden of demonstrating, by clear and convincing evidence, that the asserted claims of the '514 Patent are invalid for lack of written description under § 112.

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The Court **DIRECTS** the Clerk to transmit copies of this Order to counsel of record.[21]

DATED: June 18, 2020.

/s/ Irene M. Keeley
IRENE M. KEELEY
UNITED STATES DISTRICT JUDGE

[21] Because the parties' remaining claims, counterclaims, and defenses regarding the '001 Patent are stayed until June 20, 2020 (Dkt. Nos. 288, 315 at 12, 336 at 44), the Court's decision regarding the invalidity of the asserted claims of the '514 Patent does not deny all requested relief. Accordingly, absent a request from the parties, the Court declines to enter a separate judgment order pursuant to Federal Rule of Civil Procedure 58.