IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION,

Plaintiff,

V.

ACCORD HEALTHCARE INC., ET AL.,

Defendants.

C.A. No. 18-1043-KAJ

ORDER, FINAL JUDGMENT, AND INJUNCTION

WHEREAS, this patent infringement action was brought by Novartis Pharmaceuticals Corporation ("Novartis") alleging, *inter alia*, that Abbreviated New Drug Application ("ANDA") No. 207939, submitted by defendants HEC Pharm Co., Ltd. and HEC Pharm USA Inc. (collectively, "HEC"),[1] infringed claims 1–6 of U.S. Patent No. 9,187,405 (the "'405 Patent"). (*See* D.I. 1.)

WHEREAS, HEC pled defenses and filed declaratory judgment counterclaims against Novartis alleging invalidity and non-infringement of the '405 Patent, (*see* D.I. 134);

WHEREAS, Novartis's actions against all other Defendants in this case have been settled and/or stayed;

WHEREAS, the Court held a four-day bench trial from March 2 to 5, 2020;

WHEREAS, the Court issued its Findings of Facts and Conclusions of Law on August 10, 2020 (D.I. 769); and

[1] Defendant HEC Pharm. Group was previously dismissed from the case. (*See* D.I. 122.)

WHEREAS, the stays against all remaining defendants shall be subject to disposition upon entry of judgment against HEC;

IT IS ORDERED AND ADJUDGED that:

1. Pursuant to Federal Rule of Civil Procedure 54(b), there is no just reason to delay the entry of this Final Judgment against HEC.

2. Final judgment is entered in favor of Novartis and against HEC (1) on Novartis's claims of induced and contributory infringement under 35 U.S.C. § 271(e)(2) of claims 1–6 of the '405 patent by HEC's ANDA No. 207939 and (2) on HEC's defenses and counterclaims of non-infringement and invalidity of claims 1–6 of the '405 patent, and HEC's counterclaims are dismissed with prejudice.

3. Pursuant to 35 U.S.C. § 271(e)(4)(A), the effective date of any final approval by the United States Food and Drug Administration of HEC's ANDA No. 207939 shall be a date not earlier than the expiration date of the '405 Patent, including any extensions and/or additional periods of exclusivity to that date, except to the extent subsequently (a) agreed between Novartis and HEC or (b) ordered or otherwise permitted by this Court or other tribunal. In the event HEC seeks a stay of the effect of the preceding sentence, HEC shall file and serve a motion to stay by no later than 14 calendar days after entry of this order. Any opposition shall be filed and served no later than 14 calendar days thereafter, and any reply shall be filed and served no later than 7 calendar days after any opposition. All motion papers shall comply with the rules for motions in the Local Rules for the District of Delaware, except that page limits shall be limited as follows: opening and responsive briefs are limited to 10 pages and replies to 5 pages.

4. Pursuant to 35 U.S.C. § 271(e)(4)(B), HEC, its affiliates, subsidiaries, and each of their officers, agents, servants, and employees, those acting in privity or in concert with them, and

any person or entity to whom HEC transfers ANDA No. 207939, are hereby permanently enjoined from engaging in the commercial manufacture, use, offer for sale, and/or sale in the United States and/or importation into the United States of the fingolimod product that is the subject of HEC's ANDA No. 207939 until the expiration date of the '405 Patent, including any extensions and/or additional periods of exclusivity to that date, except to the extent subsequently (a) agreed between Novartis and HEC or (b) ordered or otherwise permitted by this Court or other tribunal.

5. In the event that a party appeals this Final Judgment, any motion for attorneys' fees and/or costs, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within 60 days after final disposition of any such appeal, and the responding party shall have 60 days after filing and service to respond.

6. In the event that no party appeals this Final Judgment, any motion for attorneys' fees and/or costs, including any motion that this case is exceptional under 35 U.S.C. § 285, shall be considered timely if filed and served within 60 days after the expiration of the time for filing a notice of appeal under Fed. R. App. P. 3 and 4, and the responding party shall have 60 days after filing and service to respond.

7. In the event Novartis seeks exoneration, release, or other relief from the Preliminary Injunction bond entered in this case (D.I. 632), Novartis shall file any such motion by no later than 14 calendar days after entry of this order. Any opposition shall be filed and served no later than 14 calendar days thereafter, and any reply shall be filed and served no later than 7 calendar days after any opposition. All motion papers shall comply with the rules for motions in the Local Rules for the District of Delaware, except that page limits shall be limited as follows: opening and responsive briefs are limited to 10 pages and replies to 5 pages.

IT IS SO ORDERED this 11TH day of September, 2020

Honorable Kent A. Jordan, Third Circuit Judge
Sitting by Designation

Approved as to form and substance:

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. ACCORD HEALTHCARE INC., et al., Defendants.	)	Civil Action No. 18-1043-KAJ **FILED UNDER SEAL**

POST-TRIAL FINDINGS OF FACT AND CONCLUSIONS OF LAW

I. INTRODUCTION

Plaintiff Novartis Pharmaceuticals Corporation ("Novartis") owns Patent No. US 9,187,405 B2 ("the '405 Patent" or "the Patent"), which claims methods to treat Relapsing-Remitting multiple sclerosis ("RRMS") using a compound called "fingolimod," at a daily dosage of 0.5 mg, absent an immediately preceding loading dose. Novartis sells fingolimod under the brand name Gilenya, which the FDA approved in 2010. Defendants HEC Pharm Co., Ltd., HEC Pharm Group, and HEC Pharm USA Inc. (collectively, "HEC") submitted an Abbreviated New Drug Application ("ANDA") to the FDA, seeking approval to make fingolimod 0.5 mg capsules, a generic copy of Novartis's Gilenya product, prior to the expiration of the '405 Patent.[1]

[1] All other defendants in this case have settled with Novartis.

Novartis then brought this suit, alleging that HEC's ANDA infringes the '405 Patent. HEC, of course, disputes that. It claims that its label does not instruct physicians to omit a loading dose from the dosing regimen, so it is not practicing one of the elements of the patent claims in suit.

HEC also brought a counterclaim that the '405 Patent is invalid for lack of written description and anticipation. As to written description, HEC claims that the Patent has no written description for the negative limitation "absent an immediately preceding loading dose" or for the claimed 0.5mg daily dose. And concerning anticipation, HEC argues that the '405 Patent is anticipated by an abstract published in the Journal of Neurology and presented at the European Neurologic Society Meeting in 2006. Novartis responds that the Patent specification provides the necessary written description and that the abstract does not anticipate because it is not prior art, does not disclose the claimed invention, and is not enabled.

The parties presented their cases during a four-day bench trial from March 2-5, 2020. As explained below, I conclude that HEC is liable for contributory and induced infringement because the label for its generic version of Gilenya instructs physicians to perform each limitation in the asserted claims of the Patent. I further conclude that the Patent is not invalid. The Patent contains an adequate written description, and it was not anticipated by the abstract. The following are my findings of fact and conclusions of law.

II. FINDINGS OF FACT

A. The Parties and the Patent

1. Plaintiff Novartis is a corporation organized and existing under the laws of Delaware, having a principal place of business at 1 Health Plz, East Hanover, New Jersey 07936. (D.I. 715, Pretrial Order ("PTO") Ex. 1 ¶ 1.)

2. Defendant HEC Pharm Co., Ltd. is a corporation organized and existing under the laws of China, having a principal place of business at Binjiang Road 62, Yidu, Yichang, 443300, Hubei, China. Defendant HEC Pharm USA Inc. is a corporation organized and existing under the laws of New Jersey, having a principal place of business at 116 Village Blvd, Suite 200, Princeton, NJ 08540. (*Id.* ¶¶ 2-3.) As noted in the Introduction, *supra*, HEC Pharm Co., Ltd., HEC Pharm USA Inc., and HEC Pharm Group are referred to collectively herein as "HEC."

3. Novartis owns the '405 Patent, which claims methods to treat RRMS with 0.5 mg of fingolimod daily absent an immediately preceding loading dose. (JTX-001.) The claims of the '405 Patent, all of which are asserted in this case, are as follows:

    1. A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

2. The method according to claim 1 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

3. A method for treating Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

4. The method according to claim 3 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

5. A method for slowing progression of Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising orally administering to said subject 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, in free form or in a pharmaceutically acceptable salt form, at a daily dosage of 0.5 mg, absent an immediately preceding loading dose regimen.

6. The method according to claim 5 wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol hydrochloride is administered.

(JTX-001 at 12:48-13:10.)

4. The specification describes an example of the claimed dosing regimen in a prophetic human clinical trial ("the Prophetic Trial"), where RRMS patients receive fingolimod "at a daily dosage of 0.5" mg for at least two to six months. (*Id.* at 11:8-14.) There is

no mention of a loading dose. (*Id.*) A prophetic trial is a study that is described on paper but not actually performed. (Tr. at 734:1-736:2.) Because FDA-approved clinical trials take a long time to perform, prophetic trials are sometimes used in patent applications to explain "if the drug were effective [in humans at a dose observed to be effective in animals], how you administer it, at what dose, and how you would follow the patient on that dose to understand whether clinical benefit was being achieved." (*Id.* at 735:2-6.)

5. The specification also describes the results of an Experimental Autoimmune Encephalomyelitis experiment ("EAE" experiment). (JTX-001 at 10:32-11:2.) In the EAE experiment, disease that mimics RRMS is induced in laboratory animals called Lewis rats, with "an acute disease within 11 days, followed by an almost complete remission around day 16 and a relapse at around days 26." (*Id.* at 10:35-39.) The specification says that 0.3 mg/kg of fingolimod, given once a week, "completely inhibits the relapse phases[.]" (*Id.* at 10:62-11:2.)

6. Novartis sells fingolimod under the brand name Gilenya, which the FDA approved in 2010. Fingolimod hydrochloride is Gilenya's sole active ingredient, at a recommended dose of 0.5 mg daily administered orally in a capsule. (D.I. 715, PTO Ex. 1 ¶ 15.)

7. HEC submitted ANDA No. 207939 to the FDA under the provisions of 21 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture, use, offer for

sale, sale, and/or importation of Fingolimod 0.5 mg capsules, a generic copy of Novartis's Gilenya product, prior to the expiration of the '405 Patent. (*Id.* ¶ 17.)

8. HEC's proposed prescribing information states in the "Dosage and Administration" section of the proposed label submitted with HEC's ANDA that "[i]n adults, the recommended dosage of fingolimod capsule is 0.5 mg orally once-daily." HEC's proposed prescribing information states in the "Indications and Usage" section that "[f]ingolimod capsules are indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in patients 18 years of age and older." (*Id.* ¶¶ 19-20.)

9. Chief Judge Leonard P. Stark presided over this case before it was reassigned to me. He adopted a definition of a person of ordinary skill in the art ("POSA") which is "'a multi-disciplinary research team' that includes '1) a Ph.D. with expertise in the area of neurology and/or an M.D. having several years of clinical experience treating multiple sclerosis patients, and who would be knowledgeable about the multiple sclerosis literature,' and '2) a pharmacologist with experience in drug development.'" (*Id.* ¶ 33.)

10. He also construed the claim preambles ("A method for reducing or preventing or alleviating relapses in Relapsing-Remitting multiple sclerosis in a subject in need thereof, comprising …" (Claim 1); "A method for treating Relapsing-Remitting

multiple sclerosis in a subject in need thereof, comprising …" (Claim 3); and "A method for slowing progression of Relapsing Remitting multiple sclerosis in a subject in need thereof, comprising …" (Claim 5)) to be a limiting statement of purpose. (D.I. 561 at 5.)

11. He construed the term "daily dosage of 0.5 mg" as the amount of drug that someone takes in a given day. (*Id.* at 9.)

12. I have reviewed those conclusions and fully adopt them here.

B. The Witnesses

1. Dr. Fred Lublin, Ph.D.

13. Dr. Fred Lublin, testifying for Novartis, is a neurologist specializing in MS at the Mount Sinai Medical Center in New York. (Tr. at 107:23-108:7.) Dr. Lublin has been an MS physician for over 40 years, has treated several thousand patients during that time, and continues to treat numerous patients. (*Id.* at 108:18-109:1.) He has published over 200 peer-reviewed publications, the vast majority of which relate to MS or animal models of that disease. (*Id.* at 109:2-13.) Dr. Lublin has been involved in many MS clinical trials for various MS medications. (*Id.* at 110:17-24.)

14. Dr. Lublin was involved in the clinical trials for fingolimod. (*Id.* at 112:13-15.) He was a member of the data safety monitoring board for the Phase I trial and a member

of the advisory committee for the Phase III protocols.[2] (*Id.* at 112:16-20.) He spent approximately 18 years working on the fingolimod clinical trial. (*Id.* at 112:21-23.)

15. At trial, Dr. Lublin was received as an "expert medical doctor specializing in MS and the design [and] execution [of] clinical trials." (*Id.* at 112:24-113:5.)

2. Peter Hiestand (via deposition)

16. Peter Hiestand is one of the named inventors, along with Christian Schnell, on the '405 Patent. (*Id.* at 314:6-15.) Hiestand and Schnell collaborated on the EAE experiment described in the Patent. (*Id.* at 315:3-6, 315:21-316:7.)

17. They "were the first ones to provide proof that the compound will work at 0.5 mg, which, … was not known at the time to the persons arranging Phase III trials." (*Id.* at 332:13-17.) Hiestand and Schnell translated the low effective EAE doses they observed to the lower human dose of 0.5 mg through a proportionality analysis. (*Id.* at 319:9-321:18.)

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[2] Clinical trials are conducted in phases. A Phase I trial involves a small number of people and is studied over a short period of time to test safety and dosing. (Tr. 123:10-15.) A Phase II trial "is called a proof-of-concept study." (*Id.* at 123:23-25.) It involves more participants and lasts longer than a Phase I trial. (*Id.* at 124:1-4.) The researchers in Phase II are still assessing safety and dosing but are also assessing whether a drug may be effective. (*Id.* at 123:25-124:7.) Phase III trials "are called pivotal trials. They involve larger numbers of patients, usually over a thousand; longer periods time …. They have to have a clinical endpoint as the primary outcome measure." (*Id.* at 128:19-129:4.) "[I]f you succeed in Phase III, you usually can take that data to someone like the FDA to try and license a drug." (*Id.* at 129:5-7.)

3. <u>Christian Schnell (via deposition)</u>

18. Christian Schnell is one of the named inventors on '405 Patent. (*Id.* at 338:4-7.) He was involved in the EAE experiments that underlie the Patent. (*Id.* at 339:1-341:4.)

4. <u>Peter Waibel (via deposition)</u>

19. Peter J. Waibel is in-house legal counsel for Novartis and was deposed pursuant to Federal Rule of Civil Procedure 30(b)(6) as a designated witness for Novartis. (*Id.* at 353:17-354:1.)

5. <u>Dr. Robert Fujinami, Ph.D.</u>

20. Dr. Robert Fujinami, testifying for HEC, is a Professor in the Department of Pathology, the Vice Dean for Faculty and Academic Affairs for the University of Utah School of Medicine and is the Assistant Vice President for Academic Affairs for University of Utah Health. (*Id.* at 378:2-10.) Dr. Fujinami obtained his Ph.D. from Northwestern University and then received post-doctoral training at the Scripps Research Institute. (*Id.* at 378:25-379:9.)

21. Dr. Fujinami's primary field of research is in EAE and related immunological mechanisms that affect initiation, exacerbations, or remissions in preclinical animal models for multiple sclerosis. (*Id.* at 378:11-19.) He has experience conducting EAE experiments using Lewis rats and other animal models. (*Id.* at 379:19-380:2.)

22. At trial, Dr. Fujinami was received as an expert, as a Ph.D. with expertise in the area of neurology. (*Id.* at 382:2-8, 383:4-9.)

6. Dr. Peter Calabresi, M.D. (via deposition)

23. Dr. Peter Calabresi is an MS physician, researcher, and professor of neurology at Johns Hopkins. (*Id.* at 423:25-424:19.) He regularly treats MS patients. (*Id.* at 424:20-425:13.) He has been a principal investigator on several multiple sclerosis clinical trials. (*Id.* at 425:14-427:16.) He was the principal investigator for the fingolimod U.S. Phase III trial called "FREEDOMS II." (*Id.*) He was also on the "FREEDOMS I" steering committee, and assisted with study design, including dose selection. (*Id.* at 428:4-429:10.)

24. Dr. Calabresi explained that clinical investigators "enter into a clinical trial with . . . equipoise, where you don't really know in the beginning what the answer is going to be, and that's the reason for doing the clinical trial." (*Id.* at 428:16-429:10.) Phase III clinical trials, "or some arms" thereof, sometimes fail (*id.* 429:11-25), and the Phase III fingolimod investigators entered into that phase with "equipoise" about the 0.5 mg dose (*id.* at 437:16-22).

7. Dr. Radojka Savic, Ph.D.

25. Dr. Radojka Savic, testifying for HEC, is an Associate Professor of Bioengineering & Therapeutic Sciences in the School of Pharmacy and an Associate Professor of Pulmonary and Critical Care in the Department of Medicine at the University of California, San Francisco. (*Id.* at 466:16-467:1.) Dr. Savic obtained her Ph.D. in Pharmacometrics from the School of Pharmacy at Uppsala University in Sweden. (*Id.*

at 463:24-464:4.) After obtaining her Ph.D., Dr. Savic did post-doctoral training in biostatistics and pharmacometrics at the French Institute for Health, INSERM in Paris, France and clinical pharmacology at the School of Medicine at Stanford University. (*Id.* at 464:23-465:9.) At the same time, Dr. Savic maintained her status as a researcher in pharmacometrics at Uppsala University, where she was responsible for the entire program of modeling disease progression and PK/PD relationships in several large multiple sclerosis clinical studies for the multiple sclerosis drug Cladribine. (*Id.* at 465:10-21.)

26. At trial, Dr. Savic was received as an expert in clinical pharmacology, including developing dosing regimens between animal and human models, and in clinical trials. (*Id.* at 471:22-472:3.)

8. <u>Dr. Paul Hoffman, M.D.</u>

27. Dr. Paul Hoffman, testifying for HEC, is a senior scientist in the Department of Neurology at the University of Florida's College of Medicine and at University of Florida Health, the clinical arm of the medical school. (*Id.* at 516:15-21.) Prior to that, Dr. Hoffman worked in the Department of Veteran's Affairs for 35 years, retiring in 2015. (*Id.* at 520:12-17.) Dr. Hoffman's experience includes being a researcher in EAE, reviewing clinical trials, and having over 40 years of experience treating multiple sclerosis patients. (*Id.* at 516:15-522:3; 532:12-533:13.)

28. At trial, Dr. Hoffman was received as an expert medical doctor with particular expertise in the treatment of multiple sclerosis. (*Id.* at 525:9-526:3.)

9. Dr. Shreeram Aradhye (via deposition)

29. Dr. Shreeram Aradhye was, at the time of his deposition, the Chief Medical Officer of Novartis and, during 2003 to 2005, he was the medical lead on the first Phase III trial of fingolimod in transplant patients and the Phase III RRMS trial of fingolimod. (*Id.* at 646:16-22.)

10. Dr. Lawrence Steinman, M.D.

30. Dr. Lawrence Steinman, testifying for Novartis, is an MS physician and researcher, and a Professor of Neurology at Stanford University. (*Id.* at 684:2-8.) Dr. Steinman earned his medical degree from Harvard University in 1973, and subsequently studied under the inventor of the MS drug Copaxone®. (*Id.* at 686:3-12.) Dr. Steinman has treated over 4,000 MS patients, and has prescribed Gilenya many times. (*Id.* at 684:11-21.) He leads a laboratory at Stanford (*id.* at 685:3-5), the institution where he has been conducting MS drug research since 1975 (*id.* at 686:13-15). Research in Dr. Steinman's laboratory led to the development of an FDA-approved treatment for MS marketed as Tysabri® (natalizumab). (*Id.* at 686:16-21.)

31. Dr. Steinman also has extensive experience with the EAE model: he has conducted approximately 1,000 EAE experiments over the last 45 years (*id.* at 693:10-693:21), and has used both acute and relapsing EAE models (*id.* at 693:22-694:4). Dr.

Steinman has published over 500 peer-reviewed publication related to MS or EAE (*id.* at 685:6-12) and is the named inventor on approximately 50 patents (*id.* at 687:15-18).

32. Dr. Steinman has been involved with MS clinical trials, serving in a variety of roles, including as principal investigator and as a member of data safety monitoring boards and advisory boards. (*Id.* at 686:22-687:6.) He has advised companies on the design of clinical trials since the 1980s. (*Id.* at 687:7-14.)

33. At trial, Dr. Steinman was received as an "expert medical doctor with expertise in multiple sclerosis and drug development … including clinical trials." (*Id.* at 688:17-689:1.)

11. Dr. William Jusko, Ph.D.

34. Dr. William Jusko, testifying for Novartis, is a distinguished professor of pharmaceutical sciences at the University of Buffalo. Dr. Jusko specializes in pharmacology, and focuses on pharmacokinetics and pharmacodynamics, in particular with respect to immunosuppressants. (*Id.* at 845:12-846:14.) Dr. Jusko has published over 600 publications in peer-reviewed journals, and has been the editor-in-chief of the primary journal in his field, the Journal of Pharmacokinetics and Pharmacodynamics. (*Id.* at 846:15-847:1.) He has also received prestigious awards in the field of pharmacology. (*Id.* at 847:2-13.)

35. Dr. Jusko's laboratory has conducted pharmacokinetic and pharmacodynamics modeling and analyses for pharmaceutical companies developing immunosuppressant drugs, including for Novartis on fingolimod. (*Id.* at 848:8-24.) Dr. Jusko's studies on fingolimod involved developing complex models for fingolimod in monkeys and rats. (*Id.* at 849:7-850:22.)

36. At trial, Dr. Jusko was received as an expert in pharmacology. (*Id.* at 852:10-17.)

C. Infringement

37. HEC's ANDA included a certification that the '405 Patent is invalid, unenforceable, and/or will not be infringed by HEC's generic fingolimod product. (D.I. 715, PTO Ex. 1 ¶ 21.)

38. HEC's proposed label is materially identical to the label for Gilenya. (PTX-310; Tr. 221:8-22.)

39. HEC's proposed label instructs doctors to perform the '405 Patent's claimed methods for the purposes stated in the preambles of the claims. Those purposes are in Sections 1 and 14 of HEC's proposed label. (Tr. 223:3-225:22.)

40. With respect to the preambles of claims 1 and 5 of the Patent, HEC's product is, according to the proposed label, "indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include … relapsing-remitting disease[.]" (PTX-310.0005; Tr. 224:3-15.) The label also describes clinical trials showing the 0.5 mg dose reduced annualized relapse rates and slowed disability progression. (PTX-310.0027-

29; Tr. 224:16-225:15, 642:17-643:10.) Reducing relapses and slowing progression are the only two clinical benefits described in HEC's proposed label. (Tr. 224:16-225:2, 642:17-643:16.) The label describes those benefits when summarizing the Phase III clinical trials for RRMS. (*Id.*) Dr. Hoffman testified that he prescribes Gilenya to patients solely for the purposes described in the label's clinical trial section. (*Id.* 643:17-23.)

41. With respect to the preamble of claim 3, again, HEC's ANDA product is, according to the proposed label, "for the treatment of patients with relapsing forms of multiple sclerosis (MS), to include … relapsing remitting disease[.]" (PTX-310.0005.)

42. The Patent's claims all require the administration of 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol, which is the chemical name for fingolimod. (JTX-001, col. 12-13.) Section 11 of HEC's proposed label instructs that doctors are administering and patients are taking the drug compound fingolimod hydrochloride, and that is as claimed in the '405 Patent. (PTX-310.0020.)

43. The claims require "orally administering … [fingolimod] . . . at a daily dosage of 0.5 mg." (JTX-001, col. 12-13.) HEC's proposed label instructs that "the recommended dosage … is 0.5 mg orally once daily[.]" (PTX-310.0006; Tr. 227:2-230:7.) That is the only dose the label recommends. (Tr. 640:14-20.) Any other dose would be off-label. (*Id.* 229:17-230:4.) Other ANDA documents from HEC show that only 0.5 mg – and no more – is the recommended dose. (PTX-273.0001; Tr. 228:6-22.)

44. A loading dose is a "greater-than-normal dose that you usually use at the start of a therapy to … jump-start the levels [of a drug] in the body." (Tr. 201:13-16.) HEC's proposed label does not mention a loading dose. (*Id.* at 641:16-22.)

45. Nothing in HEC's proposed label says to prescribe anything more or less than 0.5 mg, and the label provides a caution that there is "a greater incidence of adverse reactions without additional benefit" for doses over 0.5 mg. (PTX-310.0006.)

46. Dr. Hoffman agreed that it would be very unusual to administer a loading dose with fingolimod for an off-label use. (Tr. 547:12-549:2.)

47. Dr. Lublin has prescribed Gilenya to hundreds of patients and has never given Gilenya with a loading dose. (*Id.* at 220:15-18, 230:5-7.)

48. Dr. Hoffman testified that the only clinical benefits for HEC's generic version of Gilenya would be those identified in the clinical trial section of the proposed label. (*Id.* at 642:17-643:23.) Those trials used a dose of 0.5 mg daily, without a loading dose, solely in RRMS patients. (*Id.* at 130:7-22; PTX-310.0027.)

D. Invalidity

1. Written Description

49. A person of skill in the art would understand that the Patent describes a daily dosage of 0.5 mg of fingolimod without a preceding loading dose. A person of skill would understand that the Prophetic Trial in the Patent assumes that the daily dosage of 0.5 mg is an effective treatment, and that the first dose listed in the example is the 0.5 mg

daily dose. (Tr. 753:22-754:21.) The Prophetic Trial describes how a person of skill would investigate clinical benefit in patients receiving treatment, i.e. the daily 0.5 mg dose, by seeing the patient, doing neurologic exams, and following the disease with, for instance, magnetic resonance imaging. (*Id.* at 754:22-755:22.) The Prophetic Trial describes the methods persons of skill would use to keep track of patients receiving treatment. (*Id.* at 755:23-756:15.)

50. A person of skill would understand the Prophetic Trial to disclose a method of treatment because it specifies that the purpose of the daily dose is treatment and describes how a person of skill would follow a patient for that treatment. (*Id.* at 753:22-754:15, 804:1-805:10; 863:22-864:18.) Dr. Lublin explained that the Prophetic Trial discloses a treatment purpose because subjects "initially … received treatment for two to six months" and then "remain on treatment for as long as their disease does not progress[.]" (JTX-001 11:13-14; Tr. at 233:23-235:5.) There is no placebo group. (Tr. at 235:1-5.)

51. Dr. Lublin explained that while the Prophetic Trial described in the Patent specification was not actually conducted, it provides anticipated results from treatment. (*Id.* at 242:22-243:20.) While the Prophetic Trial would be insufficient for "purposes of the FDA," (*id.* at 267:10-13), patents are viewed from "the purview of a person of ordinary skill" (*id.* at 235:13-235:18), and can be valid and enforceable

according to the terms of title 35 of the United States Code, even if other regulatory requirements may exist for approval of the drug covered by the patent in question.

52. Read as a whole, the Patent tells a person of ordinary skill in the art that the invention is about treating RRMS. (*Id.* at 858:20-861:2.) The title indicates that it speaks of a treatment for RRMS. (*Id.* at 860:5-8.) The abstract also mentions that the drug could be used to treat conditions such as multiple sclerosis. (*Id.* at 860:11-13, 20.) Dr. Hoffman agreed that the title and specification of the '405 Patent tell persons of ordinary skill in the art that the invention is about using S1P receptor modulators, including fingolimod, for treating RRMS. (*Id.* at 597:2-10, 619:16-620:6.)

53. The two examples, animal and human, are "complementary" when read together in the context of the entire Patent. (*Id.* at 864:19-24.) Dr. Lublin testified that the Prophetic Trial shows a treatment purpose because, "when you read the patent, . . . in the animal experiment they said we've got it; a lower dose of fingolimod will work. They … make the conversion to human dosing, and then they show this clinical trial and that they're treating it. That's how I read the patent." (*Id.* at 235:19-236:8.)

54. A person of skill would understand that the inventors used a relapsing EAE model. The section of the '405 Patent reporting the experimental results is "In Vivo: Relapsing Experimental Autoimmune Encephalomyelitis (EAE)." (JTX-001.0007 at 10:32-33.) Dr. Hoffman agrees that a person of skill would understand the EAE example to describe a relapsing model, not an acute model. (Tr. 625:19-626:4,

627:15-629:10.) A person of skill would understand the inhibition of relapses could be achieved by any of the dosing schedules described in the EAE example, including the 0.3 mg/kg per week dose. (*Id.* at 629:19-630:16.)

55. A person of skill would understand that the Lewis rat animal model is a good model for relapsing EAE. (*Id.* at 838:9-840:19; *see also* 324:23-325:15.) A person of skill would also understand that EAE was the dominant model for studying MS treatments, and that results in EAE were reasonably correlated to results in humans. (*Id.* at 776: 10-13, 639:10-12; PTX-095.001.)

56. The EAE experimental results set forth in the Patent report an effective dose of 0.3 mg/kg weekly. (JTX-001 at 11:2.) According to Dr. Steinman, a person of skill in the art would have converted the 0.3 mg/kg weekly dose to 0.042 mg/kg daily, in order to compare the daily dose with the lowest known effective daily dose. (Tr. at 747:6-748:19.) Dr. Jusko explained that dividing by 7 to go from a weekly to a daily dose is appropriate because fingolimod has a very long half-life, distributes extensively, and stays in brain tissue for a long time. (*Id.* at 865:12-24, 904:2-904:18.) The method for equalizing exposure between single and multiple doses is well understood and straightforward since the dynamics of lymphocyte suppression were known to be slow. (*Id.* at 866:18-867:4.)

57. According to Dr. Jusko, when reading the EAE experimental results reported in the Patent, a person of skill would immediately recognize that 0.3 mg/kg weekly (0.042

mg/kg daily) in rats is lower than the lowest known effective dose in the prior art (0.1 mg/kg daily). (*Id.* at 862:25-863:21.) It is approximately 60% lower. (Id. at 865:23-24.)

58. A person of skill would understand that the EAE results in the '405 Patent therefore demonstrate that a proportionally lower dose (again, roughly 60% lower) could be effective in humans. (*Id.* at 865:4-867:4, 902:17-907:8.) It was understood from the results of the Phase II trial of fingolimod in patients with RRMS that the lowest known effective dose in humans was 1.25 mg daily. (*Id.* at 706:7-17, 114:17-23.) A 60% lower dose is the 0.5 mg dose described in the Patent. (*Id.*) According to Dr. Jusko, "[w]ith the extensive studies done in the animal model, the appreciable information of some of the pharmacokinetics and some of the pharmacodynamics of humans, the two systems [– animal and human –] were highly in agreement." (*Id.* at 866:10-14.)

59. Dr. Steinman agrees that a person of ordinary skill in the art would understand that the inventors translated the lowest dose that had ever been seen as effective from their EAE experiment (0.3 mg/kg once per week) to the 0.5 dose. (*Id.* at 778:25-779:14.) The Prophetic Trial would confirm to a person of skill that the inventors did a translation from their EAE experiments to the 0.5 mg daily dose in humans, as exemplified in the Patent. (*Id.* at 865:25-866:9.) It appears that the inventors chose

the lowest effective dose, which is the once-weekly regimen, for illustration in the Prophetic Trial. (*Id.* at 257:25-258:10.)

60. A person of skill would understand that the inventors were in possession of the claimed method, based on their innovative EAE experiments, understanding of the mechanism of action, using a well-established model, and the correlation to humans due to "extensive studies done with fingolimod between animals and humans." (*Id.* at 870:20-871:3.)

61. There was no recitation of a loading dose in the specification. (*Id.* at 766:16-767:2.) The Prophetic Trial describes the dosing regimen (dosage, frequency, and length) and does not involve a loading dose. (*Id.* at 214:10-215:11.) The absence of an immediately preceding loading dose from the specification, and from the Prophetic Trial, would tell a person of skill that loading doses are excluded from the invention.

62. The Prophetic Trial describes giving a "daily dosage of 0.5 . . . mg" fingolimod to treat RRMS, started "initially." (JTX-001 at 11:8-13.) The Prophetic Trial tells a person of skill that on day 1, treatment begins with a daily dose of 0.5 mg, not a loading dose. (Tr. at 765:5-766:2.) If a loading dose were directed, the Patent would say that a loading dose should be administered "initially." (*Id.* at 756:16-757:8 ("[I]t was zero out of two places where they . . . necessarily would have put it in."); *id.* at 863:22-864:18 ("They specified [an] initial regimen that does not include a loading dose.").)

63. A loading dose is necessarily a higher-than-daily dose. (*Id.* at 766:4-766:6.) On this record, starting with a daily dose plainly implies that there is no loading dose. (*Id.* at 766:7-15.) Dr. Hoffman agreed that a loading dose is usually given "as the first dose[.]" (*Id.* at 547:12-18.)

64. The EAE example discloses a dosing regimen which does not involve a loading dose. (*Id.* at 767:3-5; 215:16-21.) Dr. Hoffman, testifying for HEC, agreed. (*Id.* at 631:18-22.)

65. The Patent describes alternative dosing regimens, like "intermittent dosing," but does not describe loading doses. (*Id.* at 617:12-617:23.)

66. A person of skill in 2006 would not expect a loading dose to be used to treat RRMS with fingolimod. (*Id.* at 548:2-549:2, 551:6-12.)

2. Anticipation

67. The abstract published in the Journal of Neurology and presented at the European Neurologic Society Meeting in 2006, *Design of a randomized, placebo-controlled study of oral fingolimod (FFTY720) in relapsing-remitting multiple sclerosis* ("Kappos 2006"), and dated Mary 27-31, 2006, does not anticipate the Patent. (DTX-047; Tr. 186:2-9.) Kappos 2006 announces an upcoming Phase III trial of 1.25 mg and 0.5 mg doses of fingolimod daily compared to a placebo. (DTX-009.)

68. First, there is insufficient evidence to establish Kappos 2006 as prior art, as it has not been shown to have been available before June 27, 2006.[3] A copy of Kappos 2006 with a declaration from an employee from the British Library was offered but not admitted into evidence. The declaration is inadmissible hearsay and, in any event, is internally inconsistent regarding the location and availability of the document. (Tr. at 372:15-16; DTX-009.) The library stamp on the cover of the journal refers to a "Document Supply Centre," while the declaration refers instead to a "reading room." (Tr. at 367:23-370:21; DTX-009.)

69. The declarant, Rupert Lee, was not present at trial and not available for deposition. His declaration states that his "knowledge of the records and record keeping practices and procedures of the Library [] relies to some extent on information collated by a third party." (DTX-9.00001; *see also* Tr. at 369:20-370:6.) Mr. Lee admits that he

[3] The parties agree that June 2006 is the relevant time period for when prior art had to be publicly available in order to anticipate the patent. (*Compare* Tr. 43:25-44:2, 44:13-14, *with* Tr. 984:2-7, *and* 813:6-8.) The inventors filed a patent application in Great Britain on June 27, 2006. A Patent Cooperation Treaty application was filed on June 25, 2007. That application was translated and filed in the United States Patent and Trademark Office as U.S. Serial No. 12/303,765 (the "'765 Application"). The '405 Patent is a division of U.S. Application No. 13/149,468, filed on May 31, 2011, which is a continuation of the '765 Application. (D.I. 715, PTO Ex. 1 ¶ 13.) Based on the pre-America Invents Act 35 U.S.C. § 102(b), HEC says that publications are prior art only if published more than a year before the United States filing, so June 25, 2006. (D.I. 748 at 3.) Novartis says that the priority date, and thus the relevant date to determine if a document is prior art, is when the patent was filed in Great Britain – June 27, 2006. (D.I. 758 at 28.) For purposes of analysis, I can accept either June 25 or June 27, 2006 as the relevant date. Despite HEC advocating for June 25, it appears that June 27 is the more favorable date for HEC.

was not involved in the cataloging process for Kappos 2006, and his declaration was made 12 years after the event. (DTX-9.00001-00002.)

70. Mr. Lee does not provide any information on the procedures for cataloging, indexing, or shelving. For instance, there is no information about: (1) the cataloging process; (2) what happens to a reference once it is cataloged; (3) how the reference gets to a publicly accessible location; (4) who was responsible for carrying out such procedures; (5) how long such procedures would have taken; (6) how the reference would have been identified or indexed in a reading room; (7) how the existence of the reference would have been made known to the public; (8) how an interested person would search for the reference. (DTX-009.)

71. No evidence was admitted that shows that Kappos 2006 was publicly accessible prior to June 27, 2006. Although witnesses testified that it is typical that such abstracts are printed in advance of the meeting and in conjunction with a presentation at the meeting, there was no testimony verifying that this abstract was actually publicly available or that it accompanied a presentation.[4] (Tr. at 441:2-442:8; 672:9-673:5.)

72. Kappos 2006 was separately admitted into evidence, without the British Library declaration, as DTX-047. The abstract describes a "study of oral fingolimod

[4] Although Dr. Aradhye said that the abstract was prepared "in anticipation" of the meeting at which it was presented, (Tr. at 672:19-24,) that does not say when it became publicly available, nor does Dr. Calabresi's acknowledgement that abstracts are published in conjunction with meetings.

(FTY720) in relapsing-remitting multiple sclerosis[.]" (DTX-47.00001-00002.) It suggests three test groups, with dosing levels at 1.25 mg, 0.5 mg, and placebo, in a "randomized, double-blind" study. (DTX-47.00002-00003.)

73. Kappos 2006 does not describe a treatment for RRMS, but rather articulates a test or drug trial. (Tr. at 240:21-23.) To a person of ordinary skill in the art, "[t]esting is not treating." (*Id.* at 175:25-176:1.) The abstract offers no evidence of effectiveness, which a person of skill would look for as an indication of a treatment purpose. (*Id.* at 176:24-177:9.) The inclusion of a placebo group, which involves no treatment of RRMS, further demonstrates that the abstract describes a trial with unknown results. (*Id.* at 176:24-177:9; 895:11-896:5.)

74. Kappos 2006 does not mention a loading dose. (*Id.* at 674:9-11; 894:10-12.) Unlike a patent, which is presumed complete, an abstract of an academic paper is not presumed to contain all of the necessary information about the study. (*Id.* at 204:16-205:1; 897:1-3.) The failure to mention a loading dose does not, therefore, indicate that the dose was not present in the trial, but only that the presence or absence of a loading dose was not mentioned in the abstract. (*Id.* at 896:18-898:10.)

75. Kappos 2006 does not enable the use of 0.5 mg daily to treat RRMS because it would require undue experimentation. (*Id.* at 210:11-212:13.) "MS is a rather unpredictable disease which makes studying it all the more difficult." (*Id.* at 211:25-212:1.)

Kappos does not contain any data, like an EAE study, to indicate that a lower dosage of fingolimod would work in the treatment of RRMS. (*Id.* at 212:9-13.)

76. The prior art did not tell a person of ordinary skill that a dose of 0.5 mg was likely to work. It was known in the literature that, for a drug to be effective, it has to achieve a certain level of lymphocyte depletion, and that "the dose-response relationship is very steep[,]" meaning that, if the dose was not high enough, the drug would provide no benefit. (*Id.* at 891:10-892:6.)

III. CONCLUSIONS OF LAW

A. Infringement

1. Under the Hatch-Waxman Act, "[i]t shall be an act of infringement to submit an [ANDA] . . . for a drug . . . the use of which is claimed in a patent, . . . if the purpose of such submission is to obtain approval . . . to engage in the commercial manufacture, use, or sale of a drug . . . before the expiration of such patent." 35 U.S.C. § 271(e)(2)(A).

2. "[T]he substantive determination whether actual infringement or inducement will take place is determined by traditional patent infringement analysis, just the same as it is in other infringement suits[,]" including those under 35 U.S.C. §§ 271(a)-(c). *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003).

3. "[A] patentee seeking relief under § 271(e)(2) must prove by a preponderance of the evidence that what is to be sold will infringe." *Id.* at 1366 (internal quotation marks and citations omitted).

4. Any physician following and prescribing fingolimod according to HEC's proposed label will directly infringe.

1. Induced Infringement

5. "Whoever actively induces infringement of a patent shall be liable as an infringer." 35 U.S.C. § 271(b). "To prove induced infringement, the patentee must show direct infringement, and that the alleged infringer knowingly induced infringement and possessed specific intent to encourage another's infringement." *Toshiba Corp. v. Imation Corp.*, 681 F.3d 1358, 1363 (Fed. Cir. 2012) (internal quotation marks omitted). In the ANDA context, in which the accused product is not yet on the market, the patentee only need show infringement will occur in the future. *Warner-Lambert Co.*, 316 F.3d at 1365-66.

6. The content of the accused infringer's proposed product label controls the induced infringement inquiry, and "[t]he pertinent question is whether the … label instructs users to perform the patented method." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010). "The mere existence of direct infringement by physicians, while necessary to find liability for induced infringement, is not sufficient

for inducement." *Takeda Pharm. U.S.A., Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015).

7. "FDA regulations provide guidance on how to interpret a label." *BTG Int'l Ltd. v. Amneal Pharm. LLC*, 352 F. Supp. 3d 352, 391 (D.N.J. 2018). Pursuant to such regulations, the label must contain complete instructions on dosing and administration. *See* 21 C.F.R. 201.57.

8. "[W]here a product has substantial noninfringing uses, intent to induce infringement cannot be inferred even when the alleged inducer has actual knowledge that some users of its product may be infringing the patent." *AstraZeneca*, 633 F.3d at 1059 (Fed. Cir. 2010) (internal quotation marks and alterations omitted). "Evidence of active steps … taken to encourage direct infringement, such as advertising an infringing use or instructing how to engage in an infringing use, show[s] an affirmative intent that the product be used to infringe[.]" *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005) (internal quotation marks and citation omitted).

9. HEC is liable for induced infringement. HEC's proposed label instructs the user to perform every element of the patented method, demonstrating knowing inducement. (*See* Findings of Fact ("FF") ¶¶ 40-48.) The prescribing physician would understand the label to contain the complete dosing information, and the instructions dictate the dose of the drug in question exactly as in the Patent – 0.5 mg daily without a loading

dose. (*See* FF ¶¶ 43-48.) If a user follows the instructions, there will be direct infringement. Instructing use that will infringe is an active step that demonstrates a specific intent to infringe.

2. Contributory Infringement

10. As pertinent here, contributory infringement is found where: (1) there is direct infringement; (2) the accused infringer had knowledge of the patent at issue; and (3) the product has no substantial non-infringing uses. *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1320 (Fed. Cir. 2009); 35 U.S.C. § 271(c).

11. Unlike induced infringement, the mental state required for contributory infringement is mere knowledge of infringement, not necessarily intent to cause infringement. *Lifetime Indus., Inc. v. Trim-Lok, Inc.*, 869 F.3d 1372, 1381 (Fed. Cir. 2017).

12. "A noninfringing use is substantial when it is not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Gruenthal GMBH v. Alkem Labs. Ltd.*, 919 F.3d 1333, 1340 (Fed. Cir. 2019) (citations and internal quotation marks omitted). "In a pharmaceutical case, the noninfringing use must be in accordance with the use for which the product is indicated." *Id.*

13. The patentee must make a prima facie showing that a product is not "suitable for substantial non-infringing use[.]" *Golden Blount, Inc. v. Robert H. Peterson Co.*, 438 F.3d 1354, 1363 (Fed. Cir. 2006). Once the patentee makes out a prima facie case,

the burden of production shifts to the accused infringer to introduce evidence to demonstrate otherwise. *Id.* at 1363-64.

14. HEC is liable for contributory infringement. HEC knew of the '405 Patent and the treatment method it sets forth. (*See* FF ¶¶ 38-40.) Because the only uses for HEC's generic fingolimod product are those identified in the clinical trial section of the proposed label, there is no substantial non-infringing use for which the product is indicated. (*See* FF ¶¶ 40-43.) If a user follows the instructions on the label, there will be direct infringement.

B. Invalidity

15. "A patent is presumed to be valid, and this presumption only can be overcome by clear and convincing evidence to the contrary." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1354 (Fed. Cir. 2010) (en banc) (internal quotation marks and citations omitted).

16. "[T]he party challenging the patent bears the burden of proving invalidity by clear and convincing evidence." *Takeda Pharm. Co. v. Zydus Pharm. USA, Inc.*, 743 F.3d 1359, 1366 (Fed. Cir. 2014).

17. The Patent, which was filed in Great Britain in June 2006 and in the United States in June 2007 (FF ¶ 68 & n.3), is subject to the pre-America Invents Act ("AIA") standards for testing validity. *See* Leahy-Smith America Invents Act, Pub. L. No. 112–29, 125 Stat. 284, 293 (2011) (providing that the amendments made by the Act

do not take effect until 18 months after the enactment of the Act, i.e. March 16, 2013, and apply to any application for patent, and to any patent issuing thereon, that has an effective filing date after that date); 35 U.S.C. § 100(i)(B) (defining the effective filing date as the priority date).

18. The only invalidity arguments advanced by HEC are (1) that the '405 Patent has an insufficient written description for the no-loading-dose limitation and for the claimed 0.5 mg daily dose; and (2) that the '405 Patent is anticipated by the Kappos 2006 reference.

1. Written Description

19. Under 35 U.S.C. § 112(a), the specification of a patent "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."

20. "[T]he test for sufficiency [of a written description] is whether the disclosure of the application relied upon reasonably conveys 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 (internal citation and quotation marks omitted).

21. "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* at 1351.

22. The factors to consider "for evaluating the adequacy of the" written description include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Id.* (quoting *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005)).

23. A person of ordinary skill in the art "is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning and usage in the field." *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998).

24. The Patent here provides a sufficient written description of the invention such that a person of ordinary skill would know that the inventors were in possession of the invention. Read as a whole, the Patent describes a daily dosage of 0.5 mg of fingolimod, without a preceding loading dose, to treat RRMS. (*See* FF ¶¶ 49-66.) A person of ordinary skill would understand that the invention contained a treatment purpose, and that the treatment is for RRMS. (*See* FF ¶¶ 50-55.) The EAE model and the Prophetic Trial demonstrate a dosage of 0.5 mg per day, a lower dosage of fingolimod than existed in the prior art. (*See* FF ¶¶ 56-60.) The EAE model and the

Prophetic Trial also both indicate to a person of ordinary skill that the claimed invention did not include the administration of a loading dose. (*See* FF ¶¶ 61-66.)

2. **Anticipation**

25. Pre-AIA 35 U.S.C. § 102(b) states that "[a] person shall be entitled to a patent unless … the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country more than one year prior to the date of the application for patent in the United States…" 35 U.S.C. § 102 (b) (2002).

26. Here, the Patent Cooperation Treaty application was filed on June 25, 2007, (FF ¶ 68 & n.3,) so any publications that pre-date June 25, 2006, are prior art to the claims of the '405 Patent under 35 U.S.C. § 102(b).[5]

1. **HEC Has Not Met Its Burden to Prove Kappos 2006 Is Prior Art**

27. "Whether an asserted anticipatory document qualifies as a 'printed publication' under § 102 is a legal conclusion based on underlying factual determinations." *Cooper Cameron Corp. v. Kvaerner Oilfield Prods., Inc.*, 291 F.3d 1317, 1321 (Fed. Cir. 2002). To qualify as a printed publication under § 102(b), the publication must be publicly accessible. *Jazz Pharm., Inc. v. Amneal Pharm., LLC*, 895 F.3d 1347, 1355 (Fed. Cir. 2018). "Public accessibility is a question of fact[.]" *Id.* at 1356.

[5] As stated in footnote 3, *supra*, the parties disagree about the date for analyzing what constitutes prior art. Even if I accept the later date of June 27, 2006, it does not matter to the analysis.

28. To be publicly accessible, the reference must be "cataloged or indexed in a meaningful way." *In re Cronyn*, 890 F.2d 1158, 1161 (Fed. Cir. 1989).

29. Hearsay is not admissible as proof of a fact unless it falls under a hearsay exception. Fed. R. Evid. 802. The residual exception to the hearsay bar provides that a hearsay statement may be admitted, even if it does not meet any other hearsay exceptions, if it "is supported by sufficient guarantees of trustworthiness" and is more probative than other pieces of evidence. Fed. R. Evid. 807. The residual hearsay exception is to be used sparingly. *United States v. Bailey*, 581 F.2d 341, 347 (3d Cir. 1978).

30. The Lee declaration was offered for the truth of the matter asserted therein and therefore is hearsay. It does not fit within one of the recognized exceptions to the rule against hearsay, nor it is supported by "sufficient guarantees of trustworthiness" to be admissible under the residual hearsay exception. Lee was not present at trial and not available for deposition, so Novartis had no opportunity to probe the trustworthiness and facts surrounding the Lee declaration. (FF ¶ 69.) The Lee declaration does not provide any information on the procedures for cataloging, indexing, or shelving and was created 12 years after the cataloging. (FF ¶¶ 69-70.)

31. HEC failed to show by clear and convincing evidence that Kappos 2006 was publicly available in June 2006 or earlier. HEC has not presented any evidence, let alone clear and convincing evidence, of how Kappos 2006 was cataloged, and so has not met its

burden to show that the reference was publicly available in June 2006 or earlier.[6] (FF ¶¶ 68-71.) HEC similarly has not shown that Kappos 2006 was otherwise publicly available. Testimony that HEC points to (*see* n.4, *supra*) certainly does not constitut clear and convincing evidence of public accessibility.

2. Even if Kappos 2006 Was Prior Art, It Does Not Anticipate the Claims of the Patent

32. "A patent is invalid for anticipation if a single prior art reference discloses each and every limitation of the claimed invention." *Schering Corp. v. Geneva Pharm.*, 339 F.3d 1373, 1377 (Fed. Cir. 2003).

33. "Moreover, a prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference." *Id.*

34. "A reference may anticipate inherently if a claim limitation that is not expressly disclosed is necessarily present, or inherent, in the single anticipating reference." *In re Montgomery*, 677 F.3d 1375, 1379-80 (Fed. Cir. 2012) (citations and internal quotation marks omitted). "The inherent result must inevitably result from the

[6] HEC's waiver argument is not well-founded, as pointed out by Novartis. In Novartis's pretrial statement of contested facts, Novartis says that HEC bears the burden of proof that the asserted prior art references are actually prior art to the '405 patent. (D.I. 715, PTO Ex. 2 ¶ 5.) In its pretrial submission, under the heading "Statement of Issues of Fact that Remain to be Litigated[,]" HEC listed one of those issues as whether Kappos 2006 is prior art. (*Id.* Ex. 3 ¶ 59.)

disclosed steps; [i]nherency ... may not be established by probabilities or possibilities." *Id.* (citations and internal quotation marks omitted).

35. "[A] patent claim cannot be anticipated by a prior art reference if the allegedly anticipatory disclosures cited as prior art are not enabled.'" *Verizon Servs. Corp. v. Cox Fibernet Va., Inc.*, 602 F.3d 1325, 1337 (Fed. Cir. 2010) (internal quotation marks and citations omitted). To be "enabled," a reference must enable one of skill in the art to make and use the invention without undue experimentation. *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988).

36. "Factors to be considered in determining whether a disclosure would require undue experimentation … include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* at 737.

37. HEC has failed to prove by clear and convincing evidence that Kappos 2006 discloses the no-loading-dose limitation. (FF ¶¶ 72, 74.) Kappos 2006 is a short abstract and does not preclude the use of a loading dose in the clinical trial it described. (FF ¶¶ 72, 74.)

38. HEC has also failed to prove that Kappos 2006 discloses the purpose limitations of the preambles. (FF ¶ 73.) Chief Judge Stark held that the claim preambles are a

limiting statement of purpose, and that the Patent is "directed toward and limited to treating MS[.]" (D.I. 561 at 8 & n.3.). Kappos 2006, on the other hand, discloses a test. A person of skill would not have read Kappos 2006 as disclosing a treatment for RRMS. As Kappos 2006 describes only an early-stage clinical trial, it is too theoretical to be enabled. (FF ¶¶ 73, 75-76.)

IV. SUMMARY OF CONCLUSIONS

For the reasons set forth herein, HEC is liable for induced and contributory infringement of the '405 Patent, and the '405 Patent is not invalid for lack of written description or anticipation. Accordingly, judgment will be entered in favor of Novartis and against HEC.

Kent A. Jordan, Circuit Judge
Sitting by designation

August 10, 2020
Wilmington, Delaware