IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BIOGEN INC. and BIOGEN MA INC.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	C.A. No. _____
	)	
SANDOZ INC., SANDOZ INTERNATIONAL GMBH, SANDOZ GMBH and POLPHARMA BIOLOGICS S.A.,	)	**REDACTED - PUBLIC VERSION**
	)	**Original Filing Date: September 9, 2022**
	)	**Redacted Filing Date: September 19, 2022**
Defendants.	)	

COMPLAINT

Plaintiffs Biogen Inc. and Biogen MA Inc. (collectively, "Biogen"), for their complaint against Defendants Sandoz Inc., Sandoz GmbH, Sandoz International GmbH (collectively, "Sandoz") and Polpharma Biologics S.A. ("Polpharma") (collectively, "Defendants"), by and through their undersigned attorneys, hereby allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under 28 U.S.C. § 1331 and the United States Patent Act, 35 U.S.C. § 100 *et seq.*, including 35 U.S.C. § 271(e)(2), and under the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202, and pursuant to the Biologics Price Competition and Innovation Act ("BPCIA"), 42 U.S.C. § 262, seeking a declaratory judgment of patent infringement.

2. Biogen brings this action to halt Sandoz's and Polpharma's past, current, and future intended infringement of Biogen's rights pursuant to the patent laws of the United States, which are set out in the following patents: U.S. 7,157,276; U.S. 7,759,117; U.S. 8,124,350; U.S. 8,318,416; U.S. 8,809,049; U.S. 8,871,449; U.S. 9,005,926; U.S. 9,096,879; U.S. 9,109,015; U.S. 9,212,379; U.S. 9,316,641; U.S. 9,493,567; U.S. 9,562,252; U.S. 9,696,307; U.S. 9,709,575; U.S.

9,790,533; U.S. 10,119,976; U.S. 10,233,245; U.S. 10,308,706; U.S. 10,444,234; U.S. 10,590,454; U.S. 10,677,803; U.S. 10,705,095; U.S. 10,844,416; U.S. 11,268,119; U.S. 11,280,794; U.S. 11,287,423; and U.S. 11,292,845.

3. The claims for patent infringement brought in this action are necessitated by Defendants' development of and stated intent to import, market, and sell in Delaware and throughout the United States a biosimilar version of Biogen's groundbreaking biologic product, Tysabri® (natalizumab) ("Tysabri")—which aids over 200,000 patients in their fights against chronic, painful, and life-threatening autoimmune diseases—by improperly exploiting Biogen's intellectual property.

4. Biogen invested many years of work and research, and billions of dollars, in acquiring, developing, testing, and commercializing Tysabri to ensure that the product, and methods by which it is used, are both effective in treating Multiple Sclerosis ("MS") and Crohn's Disease ("CD") and can be administered to patients safely. Biogen's efforts resulted not only in a groundbreaking therapeutic product, but also in innovative methods of treating patients using Tysabri, manufacturing techniques and protocols, and a qualitative assay. The United States Patent and Trademark Office ("USPTO") has recognized Biogen's innovations, awarding Biogen many patents relating to Tysabri and to Biogen's pioneering manufacturing methods, including the patents at issue in this litigation.

5. In contrast, Defendants now are seeking to reap the benefits of Biogen's hard work and success by infringing Biogen's patent rights in order to develop, market, and ultimately profit from their purported biosimilar version of Tysabri.

6. The BPCIA (42 U.S.C. § 262) permits Defendants to seek and obtain approval from the U.S. Food and Drug Administration ("FDA") to market a Tysabri biosimilar, but it does not

permit the Defendants to infringe Biogen's patents. As stated herein, Defendants' activities have already infringed Biogen's patents, and Defendants' intended activities will continue to infringe those patents and additional Biogen patents, none of which Defendants have obtained a license from Biogen.

PARTIES

7. Plaintiff Biogen Inc. is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 225 Binney Street, Cambridge, MA 02142.

8. Plaintiff Biogen MA Inc. is a corporation organized and existing under the laws of the State of Massachusetts, having its principal place of business of 225 Binney Street, Cambridge, MA 02142.

9. Biogen Inc. is the sponsor of the Biologics License Application ("BLA") for Tysabri.

10. Plaintiff Biogen MA Inc. is a wholly-owned subsidiary of Biogen Inc.

11. Biogen has been discovering, developing, manufacturing, and commercializing innovative therapies to address significant unmet medical needs for more than 40 years, with a particular focus on neurological diseases. Biogen manufactures and commercializes products for a variety of medical conditions, including numerous types of cancer, rheumatoid arthritis, MS, CD, and many other serious conditions. Biogen's innovative pipeline includes therapies directed to Alzheimer's disease, SOD-1-Amyotrophic lateral sclerosis ("ALS"), Systemic lupus erythematosus, and Major depressive disorder ("MDD"), among other disease areas. In addition, Biogen itself operates a biosimilars business unit to develop and commercialize biosimilar medicines.

12. Biogen regularly seeks and invests in patents on inventions originating from its extensive research and development activities. Among those are numerous patents that claim innovative methods of treating patients using Tysabri, methods of making treatment safer for patients and methods of manufacturing antibodies, such as Tysabri.

13. The exclusivity that these patents afford to Biogen allows it to invest in developing new and novel therapies for various diseases, including MS and CD.

14. Defendant Sandoz Inc. is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 100 College Road West, Princeton, NJ 08540.

15. Defendant Sandoz International GmbH is a corporation organized and existing under the laws of the Federal Republic of Germany, having its principal place of business at Industriestrasse 25, 83607 Holzkirchen, Germany.

16. On information and belief, Sandoz Inc. operates as a subsidiary of Sandoz International GmbH. On information and belief, Sandoz International GmbH exercises considerable control over Sandoz Inc. with respect to biosimilar products.

17. Defendant Sandoz GmbH is a corporation organized and existing under the laws of the Republic of Austria, having its principal place of business at Biochemiestrasse 10, 6250 Kundl, Austria.

18. On information and belief, Sandoz Inc. operates as a subsidiary of Sandoz GmbH. On information and belief, Sandoz GmbH exercises considerable control over Sandoz Inc. with respect to biosimilar products.

19. On information and belief, Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH operate within a division of Novartis, one of the largest pharmaceutical companies in the world.

20. Polpharma Biologics S.A. is a Polish corporation, with its principal place of business at Gdansk Science & Technology Park Trzy Lipy 3, Building A 80-172 Gdansk, Poland.

JURISDICTION AND VENUE

21. This action arises under the patent laws of the United States, 35 U.S.C. § 100, *et seq.*, and this Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

22. Venue is proper in this Court under 28 U.S.C. §§ 1391 and 1400(b). In a recent correspondence sent to Biogen, Sandoz admitted venue is proper in this Court: "As the [Abbreviated Biologic License Application ("aBLA")] applicant, Sandoz is subject to venue in the District of Delaware or the District of New Jersey."

23. This Court has personal jurisdiction over Sandoz Inc. because Sandoz Inc. is a Delaware corporation, has purposefully directed activities in the State of Delaware, and this litigation relates to or arises out of those activities. Sandoz Inc. has taken the significant step of filing an aBLA (Application Number 761322) with the FDA seeking approval of a proposed biosimilar natalizumab (also referred to as "PB006," the internal designation used by Sandoz and Polpharma for their purported biosimilar product) for the express purposes of marketing, distributing, and selling in Delaware and throughout the United States.

24. On information and belief, Sandoz Inc., Sandoz International GmbH, and Sandoz GmbH hold themselves out to the public as a singular entity. For example, Sandoz maintains an Internet website that states that the Sandoz division of the Novartis Group was established in 2003, "when Novartis united all of its generics businesses under the name Sandoz - ***a single global brand***

with a long history" (https://www.sandoz.com/about-us/who-we-are/sandoz-brand) (emphasis added). Sandoz's website is copyrighted to Sandoz International GmbH and is "intended for a global audience." *Id.* As another example of the unity of Sandoz, Sandoz aggregates and reports (through Novartis) its financial performance on a global, division-wide basis, with individual entities not reporting separate financial data or making separate financial reports to government authorities. As recently as August 25, 2022, Novartis announced its plan to spin off Sandoz into a new publicly traded, standalone company (https://www.centerforbiosimilars.com/view/novartis-to-make-sandoz-a-standalone-company). There is no public differentiation between "Sandoz," "Sandoz Inc.," "Sandoz International GmbH," or "Sandoz GmbH."

25. Sandoz, acting in partnership with Polpharma, is in the business of developing, manufacturing, marketing, and selling generic biologic products, including the proposed biosimilar version of Biogen's Tysabri product. On information and belief, Sandoz intends to distribute and sell its proposed biosimilar product in the State of Delaware and throughout the United States. On information and belief, Sandoz Inc. is the United States agent for Sandoz International GmbH and Sandoz GmbH for purposes of, *inter alia*, filing regulatory submissions to, and corresponding with the FDA.

26. Sandoz issued press releases regarding the development of its purported biosimilar. In a press release dated September 3, 2019, issued from Sandoz International GmbH's Holzkirchen, Germany headquarters, Sandoz announced that it "entered into a global commercialization agreement for a proposed natalizumab biosimilar" (https://www.sandoz.com/news/media-releases/sandoz-announces-global-deal-commercialize-proposed-biosimilar-natalizumab-key). Under the agreement, Polpharma was responsible for developing, manufacturing, and supplying the proposed biosimilar natalizumab and Sandoz would

be responsible for commercializing and distributing it in all markets upon approval, through an exclusive global license.

27. In a press release dated July 25, 2022, issued from Sandoz's offices in Basel, Switzerland, Sandoz announced that the FDA accepted its biologics license application for a proposed biosimilar natalizumab, "developed by Polpharma Biologics" (https://www.sandoz.com/news/media-releases/applications-proposed-first-kind-multiple-sclerosis-biosimilar-natalizumab).

28. Sandoz Inc. has previously submitted to the jurisdiction of this Court and availed itself of the legal protections of the State of Delaware by asserting claims and not contesting jurisdiction in the United States District Court for the District of Delaware. *See, e.g.*, *Genentech, Inc. v. Sandoz Inc.*, C.A. No. 19-00202 (D. Del. Jan. 31, 2019); *Otsuka Pharmaceutical Co., LTD. v. Sandoz Inc.*, C.A. No. 21-00580 (D. Del. Apr. 26, 2021).

29. This Court has jurisdiction over Sandoz International GmbH because Sandoz International GmbH directs and/or controls, directly or indirectly, the activities of Sandoz Inc., a Delaware corporation. On information and belief, Sandoz International GmbH and its subsidiaries, including Sandoz Inc., operate within a division of Novartis organized around the manufacture, distribution, marketing, and sale of pharmaceuticals, and particularly generic and biosimilar pharmaceuticals. On information and belief, Sandoz International GmbH exercises control over Sandoz subsidiaries, including Sandoz Inc., through a global Sandoz Executive Committee (https://www.sandoz.com/about-us/who-we-are/sandoz-leadership). Therefore, Sandoz International GmbH and Sandoz Inc. are under common ownership and control.

30. Sandoz International GmbH has been involved in the filing of the aBLA discussed herein, including at least by issuing a press release from Sandoz International GmbH's

Holzkirchen, Germany headquarters (https://www.sandoz.com/news/media-releases/sandoz-announces-global-deal-commercialize-proposed-biosimilar-natalizumab-key).

31. In the alternative, this Court has personal jurisdiction over Sandoz International GmbH pursuant to Federal Rule of Civil Procedure 4(k)(2) because Sandoz International GmbH has extensive contacts with the United States, including but not limited to the above-described contacts, is not subject to jurisdiction in any particular state, and exercising jurisdiction over Sandoz International GmbH is consistent with the laws of the United States and the United States Constitution.

32. This Court has jurisdiction over Sandoz GmbH because Sandoz GmbH directs and/or controls, directly or indirectly, the activities of Sandoz Inc., a Delaware corporation. On information and belief, Sandoz GmbH is part of the Sandoz-branded Novartis division discussed above and is a Sandoz entity specifically involved in the manufacturing and distribution of biosimilar pharmaceuticals. On information and belief, Sandoz GmbH exercises control over Sandoz subsidiaries, including Sandoz Inc., through a global Sandoz Executive Committee (https://www.sandoz.com/about-us/who-we-are/sandoz-leadership). Therefore, Sandoz GmbH and Sandoz Inc. are under common ownership and control.

33. Sandoz GmbH has extensive contacts with Sandoz Inc. and was involved, at least in part, in the filing of the aBLA discussed herein. [redacted]

34. In the alternative, this Court has personal jurisdiction over Sandoz GmbH pursuant to Federal Rule of Civil Procedure 4(k)(2) because Sandoz GmbH has extensive contacts with the United States, including but not limited to the above-described contacts, is not subject to

jurisdiction in any particular state, and exercising jurisdiction over Sandoz GmbH is consistent with the laws of the United States and the United States Constitution.

35. This Court has jurisdiction over Polpharma because Polpharma's development, manufacturing, and supply of the proposed biosimilar natalizumab establishes specific personal jurisdiction in any judicial district where the biosimilar is marketed, including the District of Delaware.

36. Polpharma collaborated extensively with Sandoz to develop, manufacture, and submit the aBLA for PB006. [redacted] Polpharma is the development partner of PB006 and was responsible, in part, for communications with the FDA regarding PB006. Polpharma, in collaboration with Sandoz, intends to import, market, offer for sale, and sell the proposed biosimilar natalizumab in Delaware and throughout the United States. 42 U.S.C. § 262(k)(2)(A)(i)(v) requires that any application for a proposed biosimilar product "shall include" information demonstrating that "the facility in which the biological product is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent." On information and belief, [redacted]

37. In the alternative, this Court has personal jurisdiction over Polpharma pursuant to Federal Rule of Civil Procedure 4(k)(2) because Polpharma has extensive contacts with the United States, including but not limited to the above-described contacts, is not subject to jurisdiction in any particular state, and exercising jurisdiction over Polpharma is consistent with the laws of the United States and the United States Constitution.

BACKGROUND

Multiple Sclerosis and Crohn's Disease

38. MS is a chronic, progressive, and disabling autoimmune disease of the central nervous system ("CNS") (the brain and spinal cord). In MS, inflammatory white blood cells (i.e., leukocytes) enter the central nervous system and preferentially attack myelin, a fatty substance that surrounds and forms a sheath around nerve fibers. MS causes gradual destruction of the myelin sheath ("demyelination"), resulting in nerve damage throughout the brain and spinal cord, leaving scar tissue called "scleroses," which can be seen on magnetic resonance imaging ("MRI") images. Depending on where in the CNS the demyelination occurs, any of a broad range of symptoms associated with MS can result, including loss of muscle control, impaired vision, blindness, incontinence, sensory abnormalities, personality changes, cognitive impairment, and disabling fatigue. MS is a cause of major disability, and most patients ultimately will require assistance walking if the disease process is not interrupted. In severe cases, MS sufferers can be confined to a wheelchair or become bedridden or die from complications associated with the disease. MS has no known cure, and until 1993, there were no disease-modifying therapies available to treat the disease.

39. CD is a chronic, autoimmune disease of the gastrointestinal ("GI") tract. In CD, lesions, ulcers, or abscesses can occur anywhere along the GI tract due to inflammation caused by auto-reactive white blood cells. CD is characterized by periods of remission and relapse, and the symptoms can be highly variable depending on which parts of the GI tract are affected. Common symptoms of CD include abdominal pain, diarrhea, weight loss, and anemia, although non-intestinal symptoms may also occur, including arthritis, bone disease, eye disease, cardiovascular disease, neurological disorders, and others. CD is associated with a higher risk of developing colorectal cancer, and can negatively impact patient quality-of-life. In some cases, surgery is

required to resect portions of the GI tract that have been severely damaged by CD, although surgery does not prevent the symptoms from recurring. CD has no known cure and treatments available prior to the approval of Tysabri for CD, mainly addressed the symptoms while doing little to affect the long-term course of the disease.

40. It is estimated that MS affects approximately 400,000 people in the U.S. and 2.1 million people worldwide, and CD affects approximately 500,000 people in the U.S., 3.2 million in Europe, and millions more worldwide.

41. Tysabri, the brand name for natalizumab, has been a life changing treatment for many patients. Tysabri is used to treat relapsing forms of MS in adults (including clinically isolated syndrome, relapsing-remitting, and active secondary progressive disease). Tysabri is also used to treat moderate to severe CD.

42. Tysabri has been touted by treating physicians as a significant improvement in the standard of care for these debilitating diseases. For example, at the 2021 American Academy of Neurology Annual Meeting, Dr. Carrie Hersh commented, "[i]n addition to its efficacy on traditional measures of MS disease activity, natalizumab has been associated with improvements in health-related quality of life, fatigue, depression, and cognitive function in both real-world and clinical trial settings[.]" (https://www.neurologylive.com/view/natalizumab-improves-social-mental-health-ms).

Development and Approval of Biogen's Tysabri Product

43. Tysabri, a humanized monoclonal antibody that targets the alpha-4 (or α4) integrin component of adhesion molecules found on many white blood cells, was launched as a new type of MS and CD treatment. Tysabri was designed to selectively inhibit immune cells in the blood stream, preventing them from passing from the blood into the CNS where they can damage nerves.

44. In 2000, Biogen partnered with Elan Corporation, plc and initiated clinical trials for Tysabri of approximately 3,000 subjects. In November 2004, Tysabri was first approved by the FDA as a treatment for MS.

45. In January 2008, Tysabri was approved for the treatment of moderate to severe CD.

46. Before Tysabri's launch in 2004, the only disease-modifying treatments available for MS were interferons, and there was a strong desire among physicians and patients for a more effective treatment. Tysabri has been lauded as a substantial innovation in the treatment of MS.

Biogen Voluntarily Withdrew Tysabri From the Market Due to PML Cases

47. In February 2005, after Tysabri was on the market, it was discovered that two individuals who had received Tysabri during clinical trials developed progressive multifocal leukoencephalopathy ("PML"). A third PML case was confirmed shortly thereafter. The occurrence of PML in these three individuals was unexpected and devastating.

48. PML is a rare but serious, and often fatal, opportunistic infection of the brain. The virus infects and destroys oligodendrocytes, leading to multifocal areas of demyelination and associated neurologic dysfunction. Symptoms of PML vary from person to person, but can include loss of balance or coordination, difficulty walking, facial drooping, central blindness or sudden changes in eyesight, personality changes, mental confusion, trouble speaking, and/or weak muscles. There are no known interventions that can reliably prevent PML or that can fully cure PML if it occurs.

49. John Cunningham polyomavirus or John Cunningham Virus ("JCV" or "JC virus"), a human polyomavirus, is common in adults, and usually harmless. Infection with JCV typically occurs during childhood and the virus can remain in a latent state in the body, typically with no apparent clinical symptoms. However, JCV reactivation can lead to PML.

50. Infection with JCV causes the body to mount an immune response, including the generation of antibodies targeting the virus, which can be referred to as "anti-JCV antibodies" (or "JCV antibodies"). Individuals infected with JCV can have both anti-JCV antibodies and DNA from the virus in their bodies.

51. Biogen swiftly reacted to the reports of cases of PML. On February 28, 2005, Biogen voluntarily withdrew Tysabri from the market.

The Re-Approval of Tysabri and Biogen's Further Innovations

52. Biogen also quickly gathered experts in the field, tapped into internal resources, and worked closely with the FDA in the hope that Biogen could continue to make Tysabri treatment safely available to patients.

53. Biogen worked with the FDA for Tysabri's re-approval to the market, and after careful consideration, the FDA brought Tysabri back to the market because of how effective it was and how superior it was to prior therapeutic options.

54. On June 5, 2006, Tysabri was approved for re-entry to the market. Upon re-entry, Tysabri included a warning on the label regarding the potential risk of PML. Biogen worked hard to develop an innovative risk-management plan to give early warning of cases of PML. Biogen also developed risk stratification algorithms and PML management strategies to facilitate more personalized decision making and safer Tysabri use. Biogen's innovative approaches to safely administering Tysabri and managing PML risk were recognized by the U.S. Patent Office, which rewarded Biogen with granted patents covering safer ways to treat MS and CD using Tysabri, as discussed in more detail below.

55. After Tysabri came back on the market, Biogen doctors and scientists continued their efforts to roll out improvements that would help ensure that Tysabri would remain safely available to patients. One key to Biogen's remedial efforts was its Tysabri Outreach: Unified

Commitment to Health ("TOUCH™") Prescribing Program ("TOUCH" or "TOUCH Program") designed to mitigate the potential risk of PML in patients receiving treatment with Tysabri. Since 2006, Tysabri has only been available through this program.

56. The TOUCH Program is a type of Risk Evaluation and Mitigation Strategy ("REMS") program that the FDA can require to help ensure that the benefits of a drug outweigh its risks. REMS programs are designed to reinforce and promote the safe use of a particular drug.

57. Biogen also worked simultaneously to address how to better predict whether a patient is at risk of developing PML while taking Tysabri.

Development of Biogen's Anti-JCV Antibody ELISA Assay

58. As part of Biogen's dedication and commitment to continually improving the safety and accessibility of Tysabri, Biogen endeavored to identify risk factors for developing PML. Biogen considered a number of different possibilities, including testing for JCV DNA and anti-JCV antibodies.

59. Before Biogen's innovations, the consensus in the scientific community was that anti-JCV antibody testing in serum would not accurately predict the potential risk of PML. This was, in part, because a significant percentage of human adults have been infected with JCV so anti-JCV antibodies were thought to be common in human sera.

60. Biogen scientists were the first to discover that testing serum for anti-JCV antibodies could actually be used to accurately assess whether patients were at risk of developing PML.

61. While antibody assays existed when Tysabri was withdrawn from the market, Biogen set out to design its own, improved test and methods of determining if a patient had a PML risk in order to increase the safety of Tysabri treatment.

62. Biogen worked to produce virus-like particles ("VLPs") on a larger scale to support its ongoing efforts. Biogen contracted with a third-party company to supply VLPs for its assay research. VLP production was, and remains, fraught with complex technical problems given the importance of very high-quality VLP reagents for JCV serological assays. The specificity of anti-JCV antibodies is highly dependent on the proper formation of the VLPs. Biogen worked tirelessly to create VLPs fit for a clinical assay in terms of scalability, characterization, purification and stability, among other essential characteristics. Biogen generated sufficient evidence to indicate that the serology assay it had been developing was promising for PML risk identification and stratification.

63. In August 2009, Biogen engaged Focus Diagnostics (which was later acquired by DiaSorin Molecular LLC), which had expertise in developing commercial assays that would meet FDA standards for use in clinical practice. By December 2009, the assay was analytically validated and patient samples were tested for anti-JCV antibodies.

64. As Biogen worked on these projects, it consulted outside experts, including some who expressed skepticism that Biogen's methods would work to accurately predict a patient's risk of developing PML.

65. Biogen persevered, confident in its innovations. Biogen's efforts culminated in January 2012 with the FDA's approval of the first and only clinically and analytically validated anti-JCV antibody assay, the Stratify™ JCV Antibody Enzyme-Linked Immunosorbent Assay ("ELISA") Test ("Stratify" or the "Stratify assay"). Biogen also applied for and was granted patents covering the Stratify assay, as discussed in more detail below.

66. Stratify includes two separate tests: a detection assay and a confirmation assay. Typically, the first test performed on a sample is the detection assay. For the detection assay, "JC

virus-like particles (VLP) are pre-coated onto … microtiter plates. Diluted serum or plasma specimens and controls are incubated in the wells to allow JCV-specific antibodies present in the specimens to react with the JC VLP antigen." The result of the detection assay is reported as an index value. "A specimen with an index value that is greater than a specified upper cut-off is reported as positive for detectable JCV-specific antibodies, whereas a specimen with an index value less than the specified lower cut-off is reported as negative for detectable JCV-specific antibodies. A specimen with an index value that is equal to or between the upper and lower cut-off values is reported as indeterminate. An indeterminate result requires further evaluation in the confirmation (inhibition) assay."

67. In the confirmation assay, the sample is first contacted with soluble JC VLP antigen in solution before being added to multi-well plates coated with the JC VLP antigen. As provided in the Stratify insert "[i]n the confirmation assay, soluble JC VLP antigen will compete with plate bound JC VLP antigen for the JCV-specific antibodies present in the serum or plasma specimens." Based on this competition, the confirmation assay is able to detect the level of anti-JCV antibodies in the sample. The results of the confirmation assay are reported as percent inhibition. "The percent inhibition is calculated to confirm presence of JCV-specific antibodies in the specimen. Specimens with a percent inhibition value that is greater than the specified cut-off are reported as positive for detectable JCV-specific antibodies, whereas specimens with percent inhibition values less than or equal to the cut-off are reported as negative for detectable JCV-specific antibodies."

68. Biogen's Stratify assay has become widely adopted in conjunction with treatment with Tysabri. By utilizing Stratify to determine patients' anti-JCV antibody status, and considering other risk factors of PML, including the duration of a patient's treatment with Tysabri and prior

immunosuppressant treatment, Tysabri therapy has become safer, more effective, and accessible to over 200,000 patients.

69. In addition to approval of the Stratify assay, FDA approved changes to the Tysabri label to highlight the significance of anti-JCV antibodies and encourage testing for anti-JCV antibodies. The Tysabri label repeatedly identifies the need to weigh the risks and benefits of treatment when deciding to initiate and/or continue treatment. One of the risk factors to be considered is the presence of anti-JCV antibodies. The established method for a clinician to assess the presence of anti-JCV antibodies is through use of the Stratify assay. Biogen's TOUCH Program also recommends blood testing for anti-JCV antibodies in connection with treatment with Tysabri. The Tysabri label and TOUCH Program expressly instruct prescribers to discontinue treatment in patients with signs or symptoms of PML.

70. In 2011, Biogen and Quest Diagnostics ("Quest") entered into a license and commercialization agreement regarding Stratify. Pursuant to the agreement, Quest is the provider of the Stratify assay for Biogen (and for Biogen only) in the U.S. during a specific exclusivity period.

71. In practice, when a prescriber orders the Stratify assay for a patient considering or taking Tysabri, Quest receives a blood sample from the patient, conducts the test, and sends the results to the patient's prescriber. Quest then sends quarterly bills to Biogen for the testing. In short, Biogen pays for every Stratify kit and corresponding test that Quest performs. Patients and their insurers (public or private) are not billed for this test. It is paid for entirely by Biogen.

72. Stratify has only been validated for use with Tysabri and not with for any other natalizumab product. Stratify includes a package insert (the "Stratify Insert") that explains the test and procedures for using the test. The Stratify Insert specifically states that "[t]he purchase of this

product includes a limited, non-transferable immunity from suit under the foregoing patent claims for using only this amount of product for clinical diagnostic testing intended for use with a patient being treated or under consideration for treatment of multiple sclerosis (MS) or Crohn's disease with Tysabri® (natalizumab). ***All other uses require a license from Biogen***." (emphasis added).

73. In addition, the Stratify Insert makes clear that "[p]atented technology in this product and its use is covered by US Patent claims and corresponding patent claims outside the US. The foregoing patent claims are licensed by DiaSorin Molecular from Biogen."

74. Biogen pays Quest millions of dollars annually to administer lab services for the Stratify assay for use by Tysabri patients and potential Tysabri patients.

Manufacturing Processes and Biogen's Innovative Antibody Manufacturing

75. Even though therapeutic antibodies represent a significant share of the biologics market, manufacturing of antibodies is well-known to be a challenging task. Among the challenges and considerations faced in the manufacturing of therapeutic antibodies is the stability, bioavailability, and immunological engagement with the desired target. This is no different for an antibody such as Tysabri.

76. One of the key challenges in the manufacturing of therapeutic antibodies is that the production is limited to cell-based expression systems which are costly and inefficient, can have varied yields depending on the product and expression system, and require downstream processing to remove biological contaminants introduced from the expression system. Biogen has developed specialized cell-based expression systems that can be used to generate high yield therapeutic antibodies, as well as specialized methods for culturing mammalian cells to improve the yield of therapeutic antibodies.

77. Once the antibody is expressed in a cell-based expression system, the antibody then needs to be purified from the harvested cell culture to remove cellular components and impurities,

to inactivate any viral components used in the manufacturing process, and to concentrate the antibody therapeutic to meet clinically acceptable standards. Many purification systems have been developed to achieve this goal, and the various purification methods have different effects on the eventual yield of the therapeutic antibody. Among the frequently used purification methods are filtration-based methods, chromatography-based methods, methods using specific chemical compounds to remove impurities, or combinations of these methods. To purify therapeutic antibodies, Biogen has developed technologies using depth filtration, specific centrifugation methods, and heavy metals. These technologies are essential for the purification of antibody therapeutics to meet clinical manufacturing standards for therapeutic antibodies set by the FDA.

78. In addition, the manufacturing process also has to ensure that the sequence and structure of the antibody is not altered during the process. This is because any changes to the sequence, structure, or conformation of the antibody during the manufacturing process can have unwanted effects on the stability and/or efficacy of the resulting antibody therapeutic. For example, the produced antibody must have the same amino acid sequence as predicted by the underlying nucleic acid sequence of the expression vector from which the antibody is expressed. To this end, Biogen has developed a method of ensuring that the protein sequence of an expressed therapeutic antibody matches the predicted protein sequence for said antibody – a vital step in ensuring that the production method produces the expected product. Full-length monoclonal antibodies have bonds known as disulfide bonds in specific locations of the antibody, which determine the structure of the antibody. In recognizing the importance of maintaining the proper structure and conformation of antibodies for use as therapeutics, Biogen has developed technologies that prevent unwanted conformational changes (including unwanted sulfide-based bonds) during the manufacturing process of therapeutic antibodies.

79. Manufacturing processes can also alter the conformation, stability, and function of an antibody by altering the glycosylation profile of the antibody. Changes to the glycosylation profile of an antibody can affect the safety and effectiveness of the therapeutic antibody in its clinical context. Glycosylation refers to the addition of sugar molecules to an antibody by cellular machinery after the antibody is expressed in the cell, also referred to as a post-translation modification. Glycosylation is a common post-translational modification for antibodies produced by mammalian cells such as Chinese hamster ovary ("CHO") cells, which are frequently used for production. In order to produce therapeutic antibodies with a desired glycosylation profile, Biogen has developed technologies to produce therapeutic antibodies having specific glycosylation profiles. These developed technologies include the use of specific chemical compounds to a cell culture medium.

80. Biogen applied for and was granted patents covering its innovative manufacturing processes, discussed in more detail below.

DEFENDANTS' aBLA PRODUCT

81. Defendants undertook the development of a proposed biosimilar to Biogen's Tysabri product, which Defendants claim will be marketed under the tradename [redacted] is the commercial tradename for the same purported natalizumab product that was referred to as PB006 during development, manufacturing, and clinical trials. On information and belief, "PB" stands for "Polpharma Biologics," indicating Polpharma's involvement with the development of Defendants' proposed biosimilar product. Biogen refers to PB006 and [redacted] interchangeably herein.

82. On [redacted], Sandoz submitted an aBLA to the FDA seeking approval under 42 U.S.C. § 262(k) to market [redacted] in the United States as a biosimilar version of Biogen's

Tysabri product to treat MS and CD. Specifically, Sandoz is seeking approval of 300 mg/15 mL natalizumab solution for intravenous administration in a single-dose vial.

83. In a press release dated July 25, 2022, Sandoz announced that the FDA accepted its biologics license application for a proposed biosimilar natalizumab, "developed by Polpharma Biologics." (https://www.sandoz.com/news/media-releases/applications-proposed-first-kind-multiple-sclerosis-biosimilar-natalizumab).

84. Defendants state that PB006 is [redacted]

85. Defendants' proposed label for [redacted]

86. Although Defendants have refused to produce to Biogen all information regarding their proposed REMS program, on information and belief, [redacted]

87. [redacted]

[redacted]

88. [redacted]

89. [redacted]

90. [redacted]

91. [redacted]

92. [redacted]

93. [redacted]

94. [redacted]

95. Novartis filed a trademark application on June 30, 2021 for CLASSIFY JCV with the USPTO. Novartis AG purports to own the trademark, and has filed its trademark in the

Pharmaceutical Products category with the following description: "medical diagnostic tests and reagents for testing bodily fluids."

THE PARTIES' EXCHANGES UNDER THE BPCIA

96. In their aBLA submitted on [redacted] Defendants have demonstrated their intention to utilize Biogen's investment of time and money in discovering and developing Tysabri. The BPCIA provides an abbreviated regulatory pathway. It does not give biosimilar applicants like Sandoz or Polpharma the right to infringe valid patents in connection with the manufacture, use, offer for sale, sale, or importation of a biologic product.

97. The BPCIA was enacted on March 23, 2010 as an abbreviated pathway for approval for follow-on biologic products. 42 U.S.C. § 262(k) provides a pathway for approval of a product that is "biosimilar" to a "reference product." A "biosimilar" product is defined by the BPCIA as a biological product that (1) "is highly similar to the reference product notwithstanding minor differences in clinically inactive components" and (2) has "no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency of the product." 42 U.S.C. § 262(i)(2).

98. To facilitate the protection of a biologic innovator's patent rights, Congress enumerated a set of pre-litigation exchanges under the BPCIA outlined in 42 U.S.C. § 262(*l*) (referred to herein as the "Patent Dance"). The procedures under subsection (*l*) are intended to ensure that the maker of an innovative biologic product that is the subject of a biosimilar application will have sufficient time and opportunity to enforce its patent rights before a biosimilar product enters the market. The BPCIA also requires that a subsection (k) applicant give at least 180 days' notice before the first commercial marketing of a biosimilar licensed by the FDA. 42 U.S.C. § 262(*l*)(8)(A). The statute specifically contemplates injunctive relief, including preliminary injunctive relief, to prevent unlawful infringement.

99. The BPCIA includes a requirement that Defendants provide Biogen a copy of their aBLA submission and such other information that describes the process or processes used to manufacture the biological product within 20 days of the FDA accepting the application for review. 42 U.S.C. § 262(*l*)(2)(A).

100. The FDA has not yet made public whether it will decide to approve Sandoz's proposed biosimilar product or the indications for which the product may be approved.

101. On June 27, 2022, Sandoz contacted Biogen [redacted] Sandoz further stated it "expects to move promptly to resolve any disputes between the parties in court[.]"

102. On July 1, 2022, Biogen disclosed to Sandoz Biogen's outside counsel pursuant to 42 U.S.C. § 262(*l*)(1)(B)(ii)(I). In its communication with Sandoz, Biogen specifically "reserve[d] the right to ask for the production of additional information, including but not limited to, information that describes the process or processes used to manufacture the biological product that is the subject of the application, as contemplated under 42 U.S.C. § 262(*l*)(2)(A)-(B)."

103. On July 21, 2022, Biogen requested additional information under 42 U.S.C. § 262(*l*)(2)(A)-(B) including information regarding Defendants' use of Biogen's Stratify assay and information that describes the process or processes used to manufacture the proposed biological product in order to assess whether a claim of patent infringement could reasonably be asserted.

104. On August 3, 2022, Sandoz responded to Biogen's request by refusing to provide any additional information, stating "Sandoz is not inclined to provide additional information at this time."

105. On August 26, 2022, pursuant to 42 U.S.C. § 262(*l*)(3)(A), Biogen provided Sandoz with its list of patents for which it believed a claim of patent infringement could be reasonably asserted against Defendants' aBLA product ("Biogen's 3A List").

106. [redacted] Sandoz further stated it would "not be providing a list or statement under 42 U.S.C. § (*l*)(3)(B)[.]"

107. Therefore, after receiving Biogen's 3A List, Defendants failed to comply with the requirements of 42 U.S.C. § 262(*l*)(3)(B)(ii) by failing to provide Biogen with respect to each patent on Biogen's 3A List, "a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of the subsection (k) applicant that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biologic product that is the subject of the subsection (k) application[.]"

108. Biogen Inc., the reference product sponsor, and its wholly-owned subsidiary Biogen MA Inc., are entitled under 42 U.S.C. § 262(*l*)(9)(B) to "bring an action under Section 2201 of Title 28, United States Code, for a declaration of infringement, validity, or enforceability of any patent included in the list described in paragraph (3)(A)[.]".

THE ASSERTED BIOGEN PATENTS

109. Biogen has applied for and obtained a wide variety of issued patents covering its inventions relating to Tysabri, including regarding therapeutic uses of Tysabri, ways of making treatment with Tysabri safer for patients and Biogen's innovative methods of manufacturing antibodies, such as Tysabri.

110. Biogen's ability to evaluate Defendants' infringement has been hindered by Defendants' decision not to provide additional information as requested under 42 U.S.C. § 262(*l*)(2)(A)-(B). To the extent Defendants (a) refused to provide to Biogen the requested information; and also (b) refused to comply with the requirements of 42 U.S.C. § 262(*l*)(3)(B)(ii) with respect to each patent on Biogen's 3A List, Biogen assumes that Defendants infringe Biogen's patents. An actual, substantial, and justiciable controversy has arisen and now exists between the parties concerning whether, *inter alia*, the proposed [redacted] product has infringed, will infringe and/or will induce infringement of one or more claims of the following patents (collectively, the "Asserted Patents").

111. In light of the foregoing, and reserving all rights, Biogen is informed and believes to the best of its present ability, and on that basis alleges, that Defendants have infringed, will infringe, have induced infringement and/or will induce infringement of the Asserted Patents, each of which is owned or exclusively licensed with the right to enforce by Biogen.

- **U.S. Patent No. 9,493,567**

112. U.S. Patent No. 9,493,567 ("the '567 patent"), entitled "Methods Of Treating Inflammatory And Autoimmune Diseases With Natalizumab," was duly and legally issued by the Patent Office on November 15, 2016, and has not expired.

113. The '567 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '567 patent is attached as Exhibit 1.

- **U.S. Patent No. 10,233,245**

114. U.S. Patent No. 10,233,245 ("the '245 patent"), entitled "Methods Of Treating Inflammatory And Autoimmune Diseases With Natalizumab," was duly and legally issued by the Patent Office on March 19, 2019, and has not expired.

115. The '245 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '245 patent is attached as Exhibit 2.

- **U.S. Patent No. 11,292,845**

116. U.S. Patent No. 11,292,845 ("the '845 patent"), entitled "Methods Of Treating Inflammatory And Autoimmune Diseases With Natalizumab," was duly and legally issued by the Patent Office on April 5, 2022, and has not expired.

117. The '845 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '845 patent is attached as Exhibit 3.

- **U.S. Patent No. U.S. 10,119,976**

118. U.S. Patent No. 10,119,976 ("the '976 patent"), entitled "Method of Assessing Risk of PML," was duly and legally issued by the Patent Office on November 6, 2018, and has not expired.

119. The '976 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '976 patent is attached as Exhibit 4.

- **U.S. Patent No. 10,677,803**

120. U.S. Patent No. 10,677,803 ("the '803 patent"), entitled "Method Of Assessing Risk Of PML," was duly and legally issued by the Patent Office on June 9, 2020, and has not expired.

121. The '803 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '803 patent is attached as Exhibit 5.

- **U.S. Patent No. 11,280,794**

122. U.S. Patent No. 11,280,794 ("the '794 patent"), entitled "Method Of Assessing Risk Of PML," was duly and legally issued by the Patent Office on March 22, 2022, and has not expired.

123. The '794 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '794 patent is attached as Exhibit 6.

- **U.S. Patent No. 9,316,641**

124. U.S. Patent No. 9,316,641 ("the '641 patent"), entitled "Assay For JC Virus Antibodies," was duly and legally issued by the Patent Office on April 19, 2016, and has not expired.

125. The '641 patent is assigned to Biogen MA Inc. and Biogen has the right to enforce it. A copy of the '641 patent is attached as Exhibit 7.

- **U.S. Patent No. 10,444,234**

126. U.S. Patent No. 10,444,234 ("the '234 patent"), entitled "Assay For JC Virus Antibodies," was duly and legally issued by the Patent Office on October 15, 2019, and has not expired.

127. The '234 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '234 patent is attached as Exhibit 8.

- **U.S. Patent No. 11,287,423**

128. U.S. Patent No. 11,287,423 ("the '423 patent"), entitled "Assay For JC Virus Antibodies," was duly and legally issued by the Patent Office on March 29, 2022, and has not expired.

129. The '423 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '423 patent is attached as Exhibit 9.

- **U.S. Patent No. 8,124,350**

130. U.S. Patent No. 8,124,350 ("the '350 patent"), entitled "Methods and Products for Evaluating An Immune Response to a Therapeutic Protein," was duly and legally issued by the Patent Office on February 28, 2012, and has not expired.

131. The '350 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '350 patent is attached as Exhibit 10.

- **U.S. Patent No. 8,871,449**

132. U.S. Patent No. 8,871,449 ("the '449 patent"), entitled "Methods and Products for Evaluating An Immune Response to a Therapeutic Protein," was duly and legally issued by the Patent Office on October 28, 2014, and has not expired.

133. The '449 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '449 patent is attached as Exhibit 11.

- **U.S. Patent No. 9,709,575**

134. U.S. Patent No. 9,709,575 ("the '575 patent"), entitled "Methods and Products for Evaluating An Immune Response to a Therapeutic Protein," was duly and legally issued by the Patent Office on July 28, 2017, and has not expired.

135. The '575 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '575 patent is attached as Exhibit 12.

- **U.S. Patent No. 10,705,095**

136. U.S. Patent No. 10,705,095 ("the '095 patent"), entitled "Methods and Products for Evaluating An Immune Response to a Therapeutic Protein," was duly and legally issued by the Patent Office on July 7, 2020, and has not expired.

137. The '095 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '095 patent is attached as Exhibit 13.

- **U.S. Patent No. 9,696,307**

138. U.S. Patent No. 9,696,307 ("the '307 patent"), entitled "Methods For The Detection Of JC Polyoma Virus," was duly and legally issued by the Patent Office on July 4, 2017, and has not expired.

139. The '307 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '307 patent is attached as Exhibit 14.

- **U.S. Patent No. 8,809,049**

140. U.S. Patent No. 8,809,049 ("the '049 patent"), entitled "Methods For Producing Mammalian Cells," was duly and legally issued by the Patent Office on August 19, 2014, and has not expired.

141. The '049 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '049 patent is attached as Exhibit 15.

- **U.S. Patent No. 10,844,416**

142. U.S. Patent No. 10,844,416 ("the '416 (2020) patent"), entitled "Manganese Supplementation For Control Of Glycosylation In Mammalian Cell Culture Process," was duly and legally issued by the Patent Office on November 24, 2020, and has not expired.

143. The '416 (2020) patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '416 (2020) patent is attached as Exhibit 16.

- **U.S. Patent No. 9,562,252**

144. U.S. Patent No. 9,562,252 ("the '252 patent"), entitled "Methods Of Preventing And Removing Trisulfide Bonds," was duly and legally issued by the Patent Office on February 7, 2017, and has not expired.

145. The '252 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '252 patent is attached as Exhibit 17.

- **U.S. Patent No. 9,790,533**

146. U.S. Patent No. 9,790,533 ("the '533 patent"), entitled "Methods Of Preventing And Removing Trisulfide Bonds," was duly and legally issued by the Patent Office on October 17, 2017, and has not expired.

147. The '533 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '533 patent is attached as Exhibit 18.

- **U.S. Patent No. 10,590,454**

148. U.S. Patent No. 10,590,454 ("the '454 patent"), entitled "Methods Of Preventing And Removing Trisulfide Bonds," was duly and legally issued by the Patent Office on March 17, 2020, and has not expired.

149. The '454 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '454 patent is attached as Exhibit 19.

- **U.S. Patent No. 9,005,926**

150. U.S. Patent No. 9,005,926 ("the '926 patent"), entitled "Methods Of Preventing And Removing Trisulfide Bonds," was duly and legally issued by the Patent Office on April 14, 2015, and has not expired.

151. The '926 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '926 patent is attached as Exhibit 20.

- **U.S. Patent No. 10,308,706**

152. U.S. Patent No. 10,308,706 ("the '706 patent"), entitled "Methods Of Preventing And Removing Trisulfide Bonds," was duly and legally issued by the Patent Office on June 4, 2019, and has not expired.

153. The '706 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '706 patent is attached as Exhibit 21.

- **U.S. Patent No. 8,318,416**

154. U.S. Patent No. 8,318,416 ("the '416 (2012) patent"), entitled "Nutrient Monitoring And Feedback Control For Increased Bioproduct Production," was duly and legally issued by the Patent Office on November 27, 2012, and has not expired.

155. The '416 (2012) patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '416 (2012) patent is attached as Exhibit 22.

- **U.S. Patent No. 9,212,379**

156. U.S. Patent No. 9,212,379 ("the '379 patent"), entitled "Nutrient Monitoring And Feedback Control For Increased Bioproduct Production," was duly and legally issued by the Patent Office on December 15, 2015, and has not expired.

157. The '379 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '379 patent is attached as Exhibit 23.

- **U.S. Patent No. 9,109,015**

158. U.S. Patent No. 9,109,015 ("the '015 patent"), entitled "Method Of Isolating Biomacromolecules Using Low pH And Divalent Cations," was duly and legally issued by the Patent Office on August 18, 2015, and has not expired.

159. The '015 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '015 patent is attached as Exhibit 24.

- **U.S. Patent No. 7,157,276**

160. U.S. Patent No. 7,157,276 ("the '276 patent"), entitled "Use Of Depth Filtration In Series With Continuous Centrifugation To Clarify Mammalian Cell Cultures," was duly and legally issued by the Patent Office on January 2, 2007, and has not expired.

161. The '276 patent is assigned to Biogen Inc. with the right to enforce it. A copy of the '276 patent is attached as Exhibit 25.

- **U.S. Patent No. 7,759,117**

162. U.S. Patent No. 7,759,117 ("the '117 patent"), entitled "Use Of Depth Filtration In Series With Continuous Centrifugation To Clarify Mammalian Cell Cultures," was duly and legally issued by the Patent Office on July 20, 2010, and has not expired.

163. The '117 patent is assigned to Biogen Inc. with the right to enforce it. A copy of the '117 patent is attached as Exhibit 26.

- **U.S. Patent No. 9,096,879**

164. U.S. Patent No. 9,096,879 ("the '879 patent"), entitled "Method Of Supplementing Culture Media To Prevent Undesirable Amino Acid Substitutions," was duly and legally issued by the Patent Office on August 4, 2015, and has not expired.

165. The '879 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '879 patent is attached as Exhibit 27.

- **U.S. Patent No. 11,268,119**

166. U.S. Patent No. 11,268,119 ("the '119 patent"), entitled "Copper Supplementation For Control Of Glycosylation In Mammalian Cell Culture Process," was duly and legally issued by the Patent Office on March 8, 2022, and has not expired.

167. The '119 patent is assigned to Biogen MA Inc. with the right to enforce it. A copy of the '119 patent is attached as Exhibit 28.

COUNT I

(Declaration of Infringement of U.S. Patent No. 9,493,567)

168. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

169. The '567 patent claims a method of treating a patient with an inflammatory or autoimmune disease.

170. Representative claim 1 of the ’567 patent recites:

> 1. A method of treating a patient with an inflammatory or autoimmune disease comprising the steps of: (a) testing the patient for the presence of anti-JC virus (JCV) antibodies by a method consisting of measuring the presence of anti-JCV antibodies in the serum or plasma of a blood sample from the patient; (b) initiating treatment of the patient tested in step (a) by administering natalizumab to the patient in the event the sample is negative for anti-JCV antibodies; (c) testing the patient treated in step (b) for indicators of progressive multifocal leukoencephalopathy (PML) by detecting the presence of JCV in the patient’s cerebrospinal fluid, or detecting clinical and/or radiologic symptoms of PML in said patient, and (d) further administering natalizumab to the patient in the absence of indicators of PML or discontinuing natalizumab treatment in the presence of indicators of PML.

171. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, either directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’567 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’567 patent.

172. Defendants, with knowledge of the ’567 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’567 patent.

173. [redacted]

174. [redacted]

[redacted]

175. [redacted]

176. [redacted]

177. [redacted]

178. [redacted]

179. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '567 patent, including at least claim 1, under 35 U.S.C. § 271(b).

180. On information and belief, Defendants have infringed one or more claims of the '567 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

181. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '567 patent.

182. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '567 patent.

183. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

184. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are

enjoined from any and all activities that would infringe or would induce infringement of the claims of the ’567 patent.

COUNT II

(Declaration of Infringement of U.S. Patent No. 10,233,245)

185. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

186. The ’245 patent claims a method of using natalizumab to treat a patient with an inflammatory or autoimmune disease.

187. Representative claim 1 of the ’245 patent recites:

> 1. A method of using natalizumab to treat a patient with an inflammatory or autoimmune disease, the method comprising: (a) testing the patient for the presence of anti-JC virus (JCV) antibodies by a method consisting of determining a presence or absence of anti-JCV antibodies in serum or plasma of a blood sample of a patient; (b) identifying the patient as having serum or plasma that is negative for anti-JCV antibodies; and (c) initiating natalizumab treatment of the patient having serum or plasma that is negative for anti-JCV antibodies, wherein the testing of (a) improves the safety of the natalizumab treatment.

188. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, either directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’245 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’245 patent.

189. Defendants, with knowledge of the ’245 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’245 patent.

190. [redacted]

[redacted]

191. [redacted]

192. [redacted]

193. [redacted]

194. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '245 patent, including at least claim 1, under 35 U.S.C. § 271(b).

195. On information and belief, Defendants have infringed one or more claims of the '245 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

196. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '245 patent.

197. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '245 patent.

198. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

199. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are

enjoined from any and all activities that would infringe or would induce infringement of the claims of the ’245 patent.

COUNT III

(Declaration of Infringement of U.S. Patent No. 11,292,845)

200. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

201. The ’845 patent claims a method of using natalizumab to treat a patient with an inflammatory or autoimmune disease.

202. Representative claim 1 of the ’845 patent recites:

> 1. A method of using natalizumab to treat a patient with an inflammatory or autoimmune disease comprising: (a) administering a pharmaceutically effective amount of natalizumab to the patient; (b) monitoring the patient for indicators of progressive multifocal leukoencephalopathy (PML), wherein the monitoring comprises detecting seroconversion and/or an increasing titer of JC virus (JCV) antibodies in the patient’s blood; and (c) discontinuing the administration of natalizumab in the presence of seroconversion and/or an increasing titer of JCV antibodies; wherein the monitoring improves the safety of the treatment.

203. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, either directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’845 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’845 patent.

204. Defendants, with knowledge of the ’845 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’845 patent.

205. [redacted]

[redacted]

206. [redacted]

[redacted]

207. [redacted]

[redacted]

208. [redacted]

[redacted]

209. [redacted]

210. [redacted]

211. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '845 patent, including at least claim 1, under 35 U.S.C. § 271(b).

212. On information and belief, Defendants have infringed one or more claims of the '845 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

213. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement,

and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '845 patent.

214. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '845 patent.

215. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

216. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '845 patent.

COUNT IV

(Infringement and Declaration of Infringement of U.S. Patent No. 10,119,976)

217. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

218. The '976 patent claims methods of assessing a patient's risk of developing PML.

219. Representative claim 1 of the '976 patent recites:

> 1. A method of evaluating a patient's risk of developing Progressive Multifocal Leukoencephalopathy (PML), the method comprising: determining a JC virus (JCV) antibody titer in a biological sample from the patient, wherein the patient has a negative prior immunosuppressant exposure classification; wherein if the titer is determined to be above a pre-determined level, the patient is determined to be at a higher risk of developing PML, and wherein if the titer is determined to be at or

below an index level of 0.9, the patient is determined to be at a lower risk of developing PML.

220. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, either directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the '976 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the '976 patent.

221. Defendants, with knowledge of the '976 patent, have an affirmative intent to actively induce others to infringe one or more claims of the '976 patent.

222. [redacted]

223. [redacted]

224. [redacted]

225. [redacted]

226. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants have infringed, are infringing, and/or will infringe one or more claims of the '976 patent, including at least claim 1, under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

227. On information and belief, Defendants have infringed one or more claims of the '976 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

228. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '976 patent.

229. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '976 patent.

230. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

231. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '976 patent.

COUNT V

(Declaration of Infringement of U.S. Patent No. 10,677,803)

232. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

233. The '803 patent claims methods of assessing a patient's risk of developing PML.

234. Representative claim 1 of the '803 patent recites:

> 1. A method of treating a subject in need thereof with an anti-VLA-4 therapy, the method comprising: a. determining an anti-JC virus (JCV) antibody titer in two or more biological samples obtained from the subject over a period of time, wherein the titer is determined to be at or below an index value of 0.9 in the two or more samples; and b. administering an anti-VLA-4 antibody to the subject, thereby treating the subject with the anti-VLA-4 therapy, wherein the subject suffers from multiple sclerosis or a relapsing form of multiple sclerosis.

235. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, either directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the '803 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the '803 patent.

236. Defendants, with knowledge of the '803 patent, have an affirmative intent to actively induce others to infringe one or more claims of the '803 patent.

237. [redacted]

238. [redacted]

239. [redacted]

240. [redacted]

241. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '803 patent, including at least claim 1, under 35 U.S.C. § 271(b).

242. On information and belief, Defendants have infringed one or more claims of the '803 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

243. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '803 patent.

244. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '803 patent.

245. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

246. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are

enjoined from any and all activities that would infringe or would induce infringement of the claims of the ’803 patent.

COUNT VI

(Declaration of Infringement of U.S. Patent No. 11,280,794)

247. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

248. The ’794 patent claims methods of assessing a patient’s risk of developing PML.

249. Representative claim 1 of the ’794 patent recites:

> 1. A method of treating a subject in need thereof with natalizumab therapy, the method comprising: a) determining an anti-JC virus (JCV) antibody titer in two or more biological samples obtained from the subject over a period of time, wherein the titer is determined to be at or below an index value of 0.9 in the two or more samples; and b) administering natalizumab to the subject, thereby treating the subject with the natalizumab therapy, wherein the subject suffers from multiple sclerosis or a relapsing form of multiple sclerosis.

250. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’794 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’794 patent.

251. Defendants, with knowledge of the ’794 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’794 patent.

252. [redacted]

253. [redacted]

254. [redacted]

255. [redacted]

256. [redacted]

257. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '794 patent, including at least claim 1, under 35 U.S.C. § 271(b).

258. On information and belief, Defendants have infringed one or more claims of the '794 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

259. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '794 patent.

260. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '794 patent.

261. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

262. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '794 patent.

COUNT VII

(Infringement and Declaration of Infringement of U.S. Patent No. 9,316,641)

263. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

264. The ’641 patent claims a method of evaluating a subject for presence of anti-JCV antibodies.

265. Representative claim 1 of the ’641 patent recites:

> 1. A method of evaluating a subject for presence of JC virus antibodies, said method comprising: a. contacting a biological sample obtained from a subject with highly purified VP1 particles (HPVLPs) in solution under conditions suitable for binding of a JC Virus (JCV) antibody in the sample to an HPVLP, thereby providing a pre-incubated sample; b. contacting the pre-incubated sample with HPVLPs immobilized on a solid substrate under conditions suitable for binding of a JCV antibody in the sample to an HPVLP; c. detecting the level of JCV antibody in the pre-incubated sample binding to the immobilized HPVLPs; and d. comparing the detected level of JCV antibody in the pre-incubated sample binding to the immobilized HPVLPs to a reference value, which corresponds to a detected level of JCV antibody in a pre-incubated control sample, wherein the pre-incubated control sample was pre-incubated in the absence of HPVLPs in solution, thereby providing a pre-incubated control sample, and wherein the pre-incubated control sample was contacted with HPVLPs immobilized on a solid substrate under conditions suitable for binding of a JCV antibody in the sample to an HPVLP thereby evaluating the subject for presence of JC virus antibodies.

266. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’641 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’641 patent.

267. Defendants, with knowledge of the ’641 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’641 patent.

268. The ’641 patent covers certain steps performed by Biogen’s Stratify assay. The assay includes two separate tests: a detection assay and a confirmation assay. For the detection assay, “JC virus-like particles (VLP) are pre-coated onto … microtiter plates. Diluted serum or plasma specimens and controls are incubated in the wells to allow JCV-specific antibodies present in the specimens to react with the JC VLP antigen.” The result of the detection assay is reported

as an index value. "A specimen with an index value that is greater than a specified upper cut-off is reported as positive for detectable JCV-specific antibodies, whereas a specimen with an index value less than the specified lower cut-off is reported as negative for detectable JCV-specific antibodies. A specimen with an index value that is equal to or between the upper and lower cut-off values is reported as indeterminate. An indeterminate result requires further evaluation in the confirmation (inhibition) assay."

269. In the confirmation assay, the sample is first contacted with soluble JC VLP antigen in solution before being added to multi-well plates coated with the JC VLP antigen. As provided in the Stratify insert "[i]n the confirmation assay, soluble JC VLP antigen will compete with plate bound JC VLP antigen for the JCV-specific antibodies present in the serum or plasma specimens." Based on this competition, the confirmation assay is able to detect the level of anti-JCV antibodies in the sample. The results of the confirmation assay are reported as percent inhibition. "The percent inhibition is calculated to confirm presence of JCV-specific antibodies in the specimen. Specimens with a percent inhibition value that is greater than the specified cut-off are reported as positive for detectable JCV-specific antibodies, whereas specimens with percent inhibition values less than or equal to the cut-off are reported as negative for detectable JCV-specific antibodies."

270. On information and belief, [redacted]

[redacted]

271. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2), Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '641 patent, including at least claim 1.

272. On information and belief, Defendants have infringed one or more claims of the '641 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

273. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '641 patent.

274. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '641 patent.

275. On information and belief, despite Defendants' knowledge of the '641 patent and their infringement thereof, Defendants willfully, wantonly, and deliberately engaged in the acts of infringement alleged herein, either individually or through the approval, direction, and control of others.

276. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

277. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '641 patent.

COUNT VIII

(Infringement and Declaration of Infringement of U.S. Patent No. 10,444,234)

278. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

279. The '234 patent claims a set of reaction mixtures and a substrate.

280. Representative claim 1 of the '234 patent recites:

> 1. A set of reaction mixtures comprising a first reaction mixture in contact with a first substrate and a second reaction mixture in contact with a second substrate, wherein the first reaction mixture comprises: i) a first aliquot of a sample from a subject; ii) soluble, non-immobilized, Highly Purified Viral-Like Particles (HPVLPs) comprising VP1 polypeptides of the JC Virus (JCV); and iii) HPVLPs immobilized to the first substrate, and the second reaction mixture comprises: i) a second aliquot of the sample from the subject; ii) substantially no soluble, non-immobilized, HPVLPs; and iii) HPVLPs immobilized to the second substrate, wherein the sample was tested in an ELISA to detect the presence or absence of

anti-JCV antibodies and was classified as indeterminate for the presence or absence of anti-JCV antibodies.

281. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1 of the '234 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the '234 patent.

282. Defendants, with knowledge of the '234 patent, have an affirmative intent to actively induce others to infringe one or more claims of the '234 patent.

283. The '234 patent covers certain steps performed by Biogen's Stratify assay. The assay includes two separate tests: a detection assay and a confirmation assay. For the detection assay, "JC virus-like particles (VLP) are pre-coated onto … microtiter plates. Diluted serum or plasma specimens and controls are incubated in the wells to allow JCV-specific antibodies present in the specimens to react with the JC VLP antigen." The result of the detection assay is reported as an index value. "A specimen with an index value that is greater than a specified upper cut-off is reported as positive for detectable JCV-specific antibodies, whereas a specimen with an index value less than the specified lower cut-off is reported as negative for detectable JCV-specific antibodies. A specimen with an index value that is equal to or between the upper and lower cut-off values is reported as indeterminate. An indeterminate result requires further evaluation in the confirmation (inhibition) assay."

284. In the confirmation assay, the sample is first contacted with soluble JC VLP antigen in solution before being added to multi-well plates coated with the JC VLP antigen. As provided in the Stratify insert "[i]n the confirmation assay, soluble JC VLP antigen will compete with plate bound JC VLP antigen for the JCV-specific antibodies present in the serum or plasma

specimens." Based on this competition, the confirmation assay is able to detect the level of anti-JCV antibodies in the sample. The results of the confirmation assay are reported as percent inhibition. "The percent inhibition is calculated to confirm presence of JCV-specific antibodies in the specimen. Specimens with a percent inhibition value that is greater than the specified cut-off are reported as positive for detectable JCV-specific antibodies, whereas specimens with percent inhibition values less than or equal to the cut-off are reported as negative for detectable JCV-specific antibodies."

285. On information and belief, [redacted]

286. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2), Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will

induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '234 patent, including at least claim 1.

287. On information and belief, Defendants have infringed one or more claims of the '234 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

288. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '234 patent.

289. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '234 patent.

290. On information and belief, despite Defendants' knowledge of the '234 patent and their infringement thereof, Defendants willfully, wantonly, and deliberately engaged in the acts of infringement alleged herein, either individually or through the approval, direction, and control of others.

291. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

292. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless

Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the ’234 patent.

COUNT IX

(Infringement and Declaration of Infringement of U.S. Patent No. 11,287,423)

293. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

294. The ’423 patent claims methods and reagents for analyzing samples for the presence of anti-JCV antibodies.

295. Representative claim 1 of the ’423 patent recites:

> 1. A reaction mixture comprising soluble JC Virus (JCV) virus-like particles (VLP), a sample of serum or plasma from a subject, and immobilized JCV VLP, wherein the immobilized JCV VLP has been coated with a blocking agent.

296. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1 of the ’423 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’423 patent.

297. Defendants’ manufacture, importation, use, sale, and/or offer to sell [redacted] in the United States has infringed, and/or will infringe, and/or will induce others to infringe, either directly or under the doctrine of equivalents, one or more claims, including at least claim 1, of Biogen’s ’423 patent.

298. Defendants, with knowledge of the ’423 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’423 patent.

299. The '423 patent covers certain steps performed by Biogen's Stratify assay. The assay includes two separate tests: a detection assay and a confirmation assay. For the detection assay, "JC virus-like particles (VLP) are pre-coated onto … microtiter plates. Diluted serum or plasma specimens and controls are incubated in the wells to allow JCV-specific antibodies present in the specimens to react with the JC VLP antigen." The result of the detection assay is reported as an index value. "A specimen with an index value that is greater than a specified upper cut-off is reported as positive for detectable JCV-specific antibodies, whereas a specimen with an index value less than the specified lower cut-off is reported as negative for detectable JCV-specific antibodies. A specimen with an index value that is equal to or between the upper and lower cut-off values is reported as indeterminate. An indeterminate result requires further evaluation in the confirmation (inhibition) assay."

300. In the confirmation assay, the sample is first contacted with soluble JC VLP antigen in solution before being added to multi-well plates coated with the JC VLP antigen. As provided in the Stratify insert "[i]n the confirmation assay, soluble JC VLP antigen will compete with plate bound JC VLP antigen for the JCV-specific antibodies present in the serum or plasma specimens." Based on this competition, the confirmation assay is able to detect the level of anti-JCV antibodies in the sample. The results of the confirmation assay are reported as percent inhibition. "The percent inhibition is calculated to confirm presence of JCV-specific antibodies in the specimen. Specimens with a percent inhibition value that is greater than the specified cut-off are reported as positive for detectable JCV-specific antibodies, whereas specimens with percent inhibition values less than or equal to the cut-off are reported as negative for detectable JCV-specific antibodies."

301. On information and belief, [redacted]

302. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2), Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '423 patent, including at least claim 1.

303. On information and belief, Defendants have infringed one or more claims of the '423 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

304. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '423 patent.

305. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '423 patent.

306. On information and belief, despite Defendants' knowledge of the '423 patent and their infringement thereof, Defendants willfully, wantonly, and deliberately engaged in the acts of infringement alleged herein, either individually or through the approval, direction, and control of others.

307. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

308. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '423 patent.

COUNT X

(Declaration of Infringement of U.S. Patent No. 8,124,350)

309. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

310. The '350 patent claims a method of detecting a reduction in therapeutic efficacy of natalizumab in a subject that has been administered natalizumab.

311. Representative claim 1 of the ’350 patent recites:

> 1. A method of detecting a reduction in therapeutic efficacy of natalizumab in a subject that has been administered natalizumab, the method comprising: performing an antibody detection assay to determine whether two or more biological samples taken at different time points from the subject contain a level of anti-natalizumab antibody that is at least a threshold level of anti-natalizumab antibody, wherein the threshold level is at least two standard deviations above a mean level of anti-natalizumab antibody measured in an untreated patient population, and, wherein the presence of the threshold level of anti-natalizumab antibody in the two or more samples indicates a reduction in, or absence of, therapeutic efficacy of natalizumab.

312. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’350 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’350 patent.

313. Defendants, with knowledge of the ’350 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’350 patent.

314. [redacted]

315. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '350 patent, including at least claim 1, under 35 U.S.C. § 271(b).

316. On information and belief, Defendants have infringed one or more claims of the '350 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

317. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '350 patent.

318. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '350 patent.

319. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

320. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are

enjoined from any and all activities that would infringe or would induce infringement of the claims of the ’350 patent.

COUNT XI

(Declaration of Infringement of U.S. Patent No. U.S. 8,871,449)

321. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

322. The ’449 patent claims a method of monitoring an immune response to natalizumab in a subject treated with natalizumab.

323. Representative claim 1 of the ’449 patent recites:

> 1. A method of monitoring an immune response to natalizumab in a subject treated with natalizumab, the method comprising: performing an antibody detection assay on a biological sample taken from a subject treated with natalizumab to determine whether the biological sample contains at least a threshold level of anti-natalizumab antibody binding activity wherein the threshold level is equal to the level of anti-natalizumab antibody binding activity present in a reference sample comprising at least 200 ng/ml of anti-natalizumab antibody, and wherein the presence of at least the threshold level of anti-natalizumab antibody binding activity in the biological sample indicates a reduction in, or absence of therapeutic efficacy of natalizumab.

324. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’449 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’449 patent.

325. Defendants, with knowledge of the ’449 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’449 patent.

326. [redacted]

[redacted]

327. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '449 patent, including at least claim 1, under 35 U.S.C. § 271(b).

328. On information and belief, Defendants have infringed one or more claims of the '449 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

329. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '449 patent.

330. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '449 patent.

331. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

332. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '449 patent.

COUNT XII

(Declaration of Infringement of U.S. Patent No. U.S. 9,709,575)

333. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

334. The '575 patent claims methods and products for detecting whether at least a threshold level of anti-natalizumab antibody binding activity is present in a biological sample.

335. Representative claim 1 of the '575 patent recites:

> 1. A method comprising: administering natalizumab to a subject; and detecting whether at least a threshold level of anti-natalizumab antibody binding activity is present in a biological sample obtained from the subject, wherein the threshold level is equal to the level of anti-natalizumab antibody binding activity present in a reference sample comprising at least 500 ng/ml of anti-natalizumab antibody.

336. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the '575 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the '575 patent.

337. Defendants, with knowledge of the '575 patent, have an affirmative intent to actively induce others to infringe one or more claims of the '575 patent.

338. [redacted]

339. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '575 patent, including at least claim 1, under 35 U.S.C. § 271(b).

340. On information and belief, Defendants have infringed one or more claims of the '575 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

341. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement,

and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '575 patent.

342. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '575 patent.

343. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

344. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '575 patent.

COUNT XIII

(Declaration of Infringement of U.S. Patent No. 10,705,095)

345. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

346. The '095 patent claims methods and products for detecting the presence or absence of at least a threshold level of anti-natalizumab antibody binding activity

347. Representative claim 1 of the '095 patent recites:

> 1. A method, comprising: (a) administering natalizumab to a subject having Multiple Sclerosis; (b) detecting in a first biological sample obtained from the subject at a first time point the presence or absence of at least a threshold level of anti-natalizumab antibody binding activity; and (c) detecting in a second biological sample obtained from the subject at a second time point the presence or absence of

at least a threshold level of anti-natalizumab antibody binding activity, wherein the threshold level is equal to the level of anti-natalizumab antibody binding activity present in a reference sample comprising at least 500 ng/ml of anti-natalizumab antibody.

348. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the '095 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the '095 patent.

349. Defendants, with knowledge of the '095 patent, have an affirmative intent to actively induce others to infringe one or more claims of the '095 patent.

350. [redacted]

351. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '095 patent, including at least claim 1, under 35 U.S.C. § 271(b).

352. On information and belief, Defendants have infringed one or more claims of the '095 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

353. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '095 patent.

354. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '095 patent.

355. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

356. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '095 patent.

COUNT XIV

(Declaration of Infringement of U.S. Patent No. 9,696,307)

357. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

358. The ’307 patent claims methods for assaying the presence or absence of antibodies that bind to a variant JCV VP1 capsid protein.

359. Representative claim 1 of the ’307 patent recites:

> 1. A method comprising: contacting a solid surface that comprises an immobilized variant John Cunningham polyomavirus (JCV) VP1 capsid protein that has arginine at a position corresponding to amino acid 122 of SEQ ID NO: 1, with a biological sample obtained from a subject; and assaying for the presence or absence of a serum antibody that binds to the immobilized variant JCV VP1 capsid protein.

360. On information and belief, Defendants have infringed, are infringing, and/or will infringe and/or have induced, are inducing, and/or will induce others to infringe, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims, including at least claim 1, of the ’307 patent, and Defendants have taken and are taking meaningful steps to infringe or to induce others to infringe the ’307 patent.

361. Defendants, with knowledge of the ’307 patent, have an affirmative intent to actively induce others to infringe one or more claims of the ’307 patent.

362. [redacted]

363. On account of Defendants’ decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, including information relating to the development of their own assay, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma’s infringement. Biogen is thus unable to provide a more detailed infringement

analysis at this time without discovery and makes the following allegations upon information and belief.

364. Based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to the indications and methods of use for [redacted] and on information and belief, in the event their aBLA is approved by the FDA, Defendants will actively induce infringement by others of one or more claims of the '307 patent, including at least claim 1, under 35 U.S.C. § 271(b).

365. On information and belief, Defendants have infringed one or more claims of the '307 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

366. An actual controversy has arisen and now exists between the parties concerning whether Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '307 patent.

367. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '307 patent.

368. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

369. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe or would induce infringement of the claims of the '307 patent.

COUNT XV

(Infringement and Declaration of Infringement of U.S. Patent No. 8,809,049)

370. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

371. The '049 patent claims a method for producing one or more CHO cells having enhanced growth characteristics.

372. Representative claim 1 of the '049 patent recites:

> 1. A method for producing one or more Chinese hamster ovary (CHO) cells having enhanced growth characteristics, said method comprising: (a) subjecting a starting population of CHO cells to one or more selection cycles comprising selective conditions; wherein said selective conditions comprise incubating said cells in a bioreactor in which less than 70% of said starting population of cells remain viable, with the proviso that said selective conditions do not comprise contacting said cells with a culture medium containing exogenously added ammonium; (b) obtaining one or more CHO cells that remain viable under said selective conditions; wherein said cells obtained from said one or more selection cycles exhibit all integral cell area (ICA) that is at least 25% greater than the corresponding ICA of said starting population of cells when said cells obtained from said one or more selection cycles and said starting population of cells are grown under the same culture conditions; and (c) inoculating said cells obtained in (b) into a bioreactor.

373. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more

detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

374. [redacted]

375. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '049 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims of the '049 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

376. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '049 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '049 patent under 35 U.S.C. § 271(g).

377. On information and belief, Defendants have infringed one or more claims of the '049 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

378. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation

into the United States of [redacted] and/or PB006 has infringed or will infringe one or more claims of the ’049 patent.

379. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the ’049 patent.

380. Defendants’ infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants’ wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

381. Moreover, Defendants’ infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the ’049 patent.

COUNT XVI

(Infringement and Declaration of Infringement of U.S. Patent No. 10,844,416)

382. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

383. The ’416 (2020) patent claims methods for achieving a predetermined glycosylation profile of an anti-alpha-4-integrin antibody.

384. Representative claim 1 of the ’416 (2020) patent recites:

> 1. A method for achieving a predetermined glycosylation profile of an anti-α4-integrin antibody, an interferon beta-1a polypeptide, or a rFVIIIFc, the method comprising: adding manganese to a cell culture at a concentration that falls within a target manganese concentration range, wherein the cell culture comprises host cells producing the anti-α4-integrin antibody, interferon beta-1a polypeptide, or rFVIIIFc, and if the manganese concentration in the cell culture is below the target manganese concentration range, the cell culture is supplemented with manganese,

wherein the target manganese concentration range in the cell culture for an anti-α4-integrin antibody, an interferon beta-1a polypeptide, or a rFVIIIFc is respectively 0.025 μM to 10 μM, 0.1 μM to 5 μM, and 30 nM to 1800 nM.

385. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

386. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '416 (2020) patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '416 (2020) patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

387. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '416 (2020) patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '416 (2020) patent under 35 U.S.C. § 271(g).

388. On information and belief, Defendants have infringed one or more claims of the '416 (2020) patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

389. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '416 (2020) patent.

390. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '416 (2020) patent.

391. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

392. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '416 (2020) patent.

COUNT XVII

(Infringement and Declaration of Infringement of U.S. Patent No. 9,562,252)

393. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

394. The ’252 patent claims methods for reducing the formation of trisulfide bonds in a protein.

395. Representative claim 1 of the ’252 patent recites:

> 1. A method for reducing the formation of trisulfide bonds in a protein comprising culturing cells expressing said protein in the presence of an effective amount of an inhibitor of cysteine degradation, whereby trisulfide linkage formation in said protein is reduced relative to cells cultured in medium without the inhibitor of cysteine degradation, and wherein said inhibitor is methyl pyruvate, ethyl pyruvate, glyceraldehyde, or glyoxylic acid.

396. On account of Defendants’ decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma’s infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006’s manufacture at this time without discovery and makes the following allegations upon information and belief.

397. Defendants have refused Biogen’s requests for information sufficient to fully evaluate whether the ’252 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the ’252 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

398. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the ’252 patent, or have done so already.

Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '252 patent under 35 U.S.C. § 271(g).

399. On information and belief, Defendants have infringed one or more claims of the '252 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

400. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '252 patent.

401. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '252 patent.

402. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

403. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '252 patent.

COUNT XVIII

(Infringement and Declaration of Infringement of U.S. Patent No. 9,790,533)

404. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

405. The ’533 patent claims a cell culture for reducing the formation of trisulfide bonds in a protein.

406. Representative claim 1 of the ’533 patent recites:

> 1. A cell culture for reducing the formation of trisulfide bonds in a protein comprising a culture medium which comprises an effective amount of an inhibitor of cysteine degradation selected from methyl pyruvate, ethyl pyruvate, glyceraldehyde, and glyoxylic acid.

407. On account of Defendants’ decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma’s infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006’s manufacture at this time without discovery and makes the following allegations upon information and belief.

408. Defendants have refused Biogen’s requests for information sufficient to fully evaluate whether the ’533 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the ’533 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

409. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the ’533 patent, or have done so already. Defendants’ making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the ’533 patent under 35 U.S.C. § 271(g).

410. On information and belief, Defendants have infringed one or more claims of the '533 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

411. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '533 patent.

412. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '533 patent.

413. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

414. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '533 patent.

COUNT XIX

(Infringement and Declaration of Infringement of U.S. Patent No. 10,590,454)

415. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

416. The '454 patent claims a method for reducing the formation of trisulfide bonds in proteins during large-scale production.

417. Representative claim 1 of the '454 patent recites:

> 1. A method for reducing the formation of trisulfide bonds in proteins during large-scale production comprising culturing cells expressing said proteins in the presence of an effective amount of an inhibitor of cysteine degradation, whereby trisulfide linkage formation in said proteins is reduced relative to cells cultured in medium without the inhibitor of cysteine degradation, wherein the inhibitor of cysteine degradation is formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, stearic acid, arachidonic acid, docosahexaenoic acid, myristoleic acid, palmitoleic acid, elaidic acid, erucic acid, vaccenic acid, penicillamine, carotenes, alpha-tocopherol, ubiquinol, lactic acid, formic acid, oxalic acid, or uric acid, and wherein said cells are mammalian cells.

418. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

419. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '454 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '454 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

420. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '454 patent, or have done so already.

Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '454 patent under 35 U.S.C. § 271(g).

421. On information and belief, Defendants have infringed one or more claims of the '454 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

422. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '454 patent.

423. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '454 patent.

424. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

425. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '454 patent.

COUNT XX

(Infringement and Declaration of Infringement of U.S. Patent No. 9,005,926)

426. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

427. The ’926 patent claims a method for converting trisulfide bonds to disulfide bonds in antibodies or antigen-binding fragments thereof and a method for reducing heat induced fragmentation in antibodies or antigen-binding fragments thereof.

428. Representative claim 1 of the ’926 patent recites:

> 1. A method for convert[ing] in in trisulfide bonds to disulfide bonds in antibodies or antigen-binding fragments thereof wherein the method comprises: (a) allowing antibodies or antigen-binding fragments thereof in a solution comprising at least one antibody or antigen-binding fragment thereof with at least one trisulfide bond linking a heavy chain constant region and a light chain constant region of the at least one antibody or antigen-binding fragment thereof to contact and associate with a solid support; (b) exposing the at least one antibody or antigen-binding fragment thereof to a reducing agent at an effective concentration to convert the trisulfide bond to a disulfide bond; and (c) removing the reducing agent from the at least one antibody or antigen-binding fragment thereof, wherein steps (a) and (b) are performed simultaneously or in any sequential order such that the reducing agent is applied to the solid support, wherein steps (a) and (b) are followed subsequently by step (c), wherein the reducing agent is selected from cysteine L-cysteine, cysteamine reduced glutathione (GSH) and L-GSH, and wherein the method reduces heat induced fragmentation in the antibodies or antigen-binding fragments thereof compared to antibodies or antigen-binding fragments not exposed to the reducing agent, wherein heat induced fragmentation is measured by denaturing, non-reducing capillary electrophoresis.

429. On account of Defendants’ decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma’s infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006’s manufacture at this time without discovery and makes the following allegations upon information and belief.

430. Defendants have refused Biogen’s requests for information sufficient to fully evaluate whether the ’926 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing

methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '926 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

431. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '926 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '926 patent under 35 U.S.C. § 271(g).

432. On information and belief, Defendants have infringed one or more claims of the '926 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

433. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '926 patent.

434. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '926 patent.

435. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

436. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '926 patent.

COUNT XXI

(Infringement and Declaration of Infringement of U.S. Patent No. 10,308,706)

437. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

438. The '706 patent claims a method for reducing the formation of trisulfide bonds in antibodies or antigen-binding fragments thereof.

439. Representative claim 1 of the '706 patent recites:

> 1. A method for reducing the formation of trisulfide bonds in antibodies or antigen-binding fragments thereof, wherein said method comprises cultivating mammalian cells producing said antibodies or antigen-binding fragments thereof in cell culture media under conditions selected from the group consisting of: (a) maintaining or reducing the concentration of sulfur or sulfur-containing compounds in the cell culture media below a threshold level of 10 millimolar; (b) harvesting the cell culture media when the cell culture is at approximately maximum cell density or at approximately peak production of the antibodies or antigen-binding fragments thereof; and (c) a combination of (a) and (b), wherein the sulfur-containing compound is selected from: (i) hydrogen sulfide; (ii) sodium sulfide; and (iii) sodium hydrogen sulfide.

440. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

441. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '706 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '706 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

442. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '706 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '706 patent under 35 U.S.C. § 271(g).

443. On information and belief, Defendants have infringed one or more claims of the '706 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

444. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '706 patent.

445. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '706 patent.

446. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

447. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '706 patent.

COUNT XXII

(Infringement and Declaration of Infringement of U.S. Patent No. 8,318,416)

448. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

449. The '416 (2012) patent claims an automated method of increasing the quantity of a bioproduct produced, or decreasing bioproduct production time, in a bioreactor cell culture process.

450. Representative claim 1 of the '416 (2012) patent recites:

> 1. An automated method of increasing the quantity of a bioproduct produced, or decreasing bioproduct production time, in a bioreactor cell culture process, the method comprising: (a) intermittently or continuously analyzing one or more amino acids in the bioreactor cell culture by means of an automated sampling device to generate data representative of the concentration of said one or more amino acids; (b) processing said data by means of a computer-based processing program to determine an amount of nutrient media to add to the bioreactor; and, (c) adding said amount of nutrient media determined in (b) to the bioreactor cell culture by means of an automated feed device when the concentration of said one or more amino acids is below a target value.

451. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of

patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

452. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '416 (2012) patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '416 (2012) patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

453. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '416 (2012) patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '416 (2012) patent under 35 U.S.C. § 271(g).

454. On information and belief, Defendants have infringed one or more claims of the '416 (2012) patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

455. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '416 (2012) patent.

456. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '416 (2012) patent.

457. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

458. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '416 (2012) patent.

COUNT XXIII

(Infringement and Declaration of Infringement of U.S. Patent No. 9,212,379)

459. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

460. The '379 patent claims an automated method of increasing the quantity of a bioproduct produced, or decreasing bioproduct production time, in a bioreactor cell culture process.

461. Representative claim 1 of the '379 patent recites:

> 1. An automated method of increasing the quantity of a bioproduct produced, or decreasing bioproduct production time, in a bioreactor cell culture process, the method comprising: (a) intermittently or continuously analyzing one or more carbohydrates or vitamins in the bioreactor cell culture by means of an automated sampling device to generate data representative of the concentration of said one or more carbohydrates or vitamins; (b) processing said data by means of a computer-based processing program to determine an amount of nutrient media to add to the bioreactor; and, (c) adding said amount of nutrient media determined in (b) to the bioreactor cell culture by means of an automated feed device when the concentration of said one or more carbohydrates or vitamins is below a target value.

462. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

463. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '379 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '379 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

464. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '379 patent, or has done so already.

Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '379 patent under 35 U.S.C. § 271(g).

465. On information and belief, Defendants have infringed one or more claims of the '379 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

466. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '379 patent.

467. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '379 patent.

468. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

469. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '379 patent.

COUNT XXIV

(Infringement and Declaration of Infringement of U.S. Patent No. 9,109,015)

470. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

471. The '015 patent claims a method of purifying a composition containing a recombinant protein and an impurity.

472. Representative claim 1 of the '015 patent recites:

> 1. A method of purifying a composition containing a recombinant protein and an impurity, the method comprising: (a) lowering the pH of the composition to a pH range of about 3.0 to about 6.5; (b) adding a divalent cation selected from the group consisting of Co^{2+}, Ni^{2+} and combinations thereof to the composition to result in a divalent cation concentration of about 1 mM to about 50 mM; and (c) separating the protein from the impurity, wherein the protein comprises an antibody or a fusion protein comprising an Fc region, which is produced by a recombinant eukaryotic host cell, wherein the composition comprises a harvest feed of the recombinant eukaryotic host cell, wherein the addition of the divalent cation increases the recovery of the protein by greater than 3% compared to the amount of protein recovered without the addition of the divalent cation, and wherein the separating of (c) is performed by subjecting the composition to centrifugation, the centrifugation forming a supernatant and a precipitate wherein the protein is substantially in the supernatant, or wherein the separating of (c) is performed by filtering the composition, the filtering forming a permeate stream and a retentate stream wherein the protein is substantially in the permeate stream, and wherein (a) and (b) are carried out sequentially in any order before (c).

473. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

474. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '015 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will

infringe one or more claims, including at least claim 1, of the '015 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

475. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '015 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '015 patent under 35 U.S.C. § 271(g).

476. On information and belief, Defendants have infringed one or more claims of the '015 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

477. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '015 patent.

478. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '015 patent.

479. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

480. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless

Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '015 patent.

COUNT XXV

(Infringement and Declaration of Infringement of U.S. Patent No. 7,157,276)

481. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

482. The '276 patent claims a method for clarification of an industrial scale cell sample.

483. Representative claim 1 of the '276 patent recites:

> 1. A method for clarification of an industrial scale cell sample comprising the steps of: (a) centrifuging a cell sample using a gravitational force within a range of about 8,000×g to about 15,000×g and a Q/Σ ratio ranging between 0.9×10^{-8} and 2.8×109 for industrial scale production of therapeutic proteins, whereby a solid phase comprising cells and debris is separated from a centrate; and (b) applying the centrate to a depth filtration means.

484. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

485. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '276 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will

infringe one or more claims, including at least claim 1, of the '276 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

486. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '276 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '276 patent under 35 U.S.C. § 271(g).

487. On information and belief, Defendants have infringed one or more claims of the '276 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

488. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '276 patent.

489. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '276 patent.

490. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

491. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless

Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '276 patent.

COUNT XXVI

(Infringement and Declaration of Infringement of U.S. Patent No. 7,759,117)

492. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

493. The '117 patent claims a method of clarifying for separating therapeutic proteins from an industrial scale cell sample.

494. Representative claim 1 of the '117 patent recites:

> 1. A method for separating therapeutic proteins from an industrial scale cell sample comprising: (a) centrifuging the cell sample at a gravitational force of from about 8,000×g to about 15,000×g and a Q/Σ ratio of about 1×10^{-8} m/s, wherein the centrifugation separates the cells and cellular debris from the centrate which comprises the therapeutic proteins; and (b) applying the centrate to a depth filtration means so as to recover a filtrate which comprises the therapeutic proteins, wherein the depth filtration means is effective to separate remaining particulate matter from the filtrate comprising the therapeutic proteins.

495. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

496. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '117 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing

methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '117 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

497. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '117 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '117 patent under 35 U.S.C. § 271(g).

498. On information and belief, Defendants have infringed one or more claims of the '117 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

499. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '117 patent.

500. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '117 patent.

501. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

502. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '117 patent.

COUNT XXVII

(Infringement and Declaration of Infringement of U.S. Patent No. 9,096,879)

503. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

504. The '879 patent claims a method of preventing misincorporation of serine in place of asparagine during translation of a polypeptide of interest in a mammalian cell.

505. Representative claim 1 of the '879 patent recites:

> 1. A method for preventing misincorporation of serine in place of asparagine during translation of a polypeptide of interest in a mammalian cell, comprising: (a) providing a culture comprising the cell in growth media, wherein the culture has a volume of at least 500 liters; (b) supplementing the culture with a feed medium comprising asparagine, or a metabolic precursor thereof, in an amount sufficient to reduce serine misincorporation; and (c) maintaining the supplemented culture under conditions appropriate for expression of the polypeptide of interest, wherein the polypeptide of interest expressed by the cell comprises less than about 3% serine misincorporated in place of asparagine.

506. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

507. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '879 patent has been or will be infringed. Therefore, based on information

presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '879 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

508. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '879 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '879 patent under 35 U.S.C. § 271(g).

509. On information and belief, Defendants have infringed one or more claims of the '879 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

510. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '879 patent.

511. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '879 patent.

512. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting

from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

513. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '879 patent.

COUNT XXVIII

(Infringement and Declaration of Infringement of U.S. Patent No. 11,268,119)

514. Biogen re-alleges and incorporates the foregoing allegations as if fully set forth herein.

515. The '119 patent claims a method for achieving a predetermined galactosylation profile of an anti-alpha-4-integrin antibody.

516. Representative claim 1 of the '119 patent recites:

> 1. A method for achieving a predetermined galactosylation profile of an anti-α4-integrin antibody comprising: culturing host cells producing the anti-α4-integrin antibody in a cell culture comprising an amount of copper within a target copper concentration range, wherein the target copper concentration range in the cell culture is between 200 nM and 500 nM, wherein the target copper concentration is achieved by supplementing the cell culture with a yeast hydrolysate comprising copper.

517. On account of Defendants' decision not to provide additional information as requested by Biogen under 42 U.S.C. § 262(*l*)(2)(A)-(B) in order to assess whether a claim of patent infringement could reasonably be asserted, Biogen is unable at this time to fully evaluate the extent of Sandoz and/or Polpharma's infringement. Biogen is thus unable to provide a more detailed infringement analysis for the process(es) of PB006's manufacture at this time without discovery and makes the following allegations upon information and belief.

518. Defendants have refused Biogen's requests for information sufficient to fully evaluate whether the '119 patent has been or will be infringed. Therefore, based on information presently available to Biogen, including without limitation, the confidential information disclosed to Biogen by Defendants pursuant to 42 U.S.C. § 262(*l*)(2) relating to PB006 manufacturing methods, and on information and belief, Defendants have infringed, are infringing, and/or will infringe one or more claims, including at least claim 1, of the '119 patent under 35 U.S.C. §§ 271(a) and/or (b), directly or indirectly, literally and/or under the doctrine of equivalents.

519. On information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States [redacted] which is made by a process that falls within the scope of one or more claims of the '119 patent, or have done so already. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States infringes one or more claims of the '119 patent under 35 U.S.C. § 271(g).

520. On information and belief, Defendants have infringed one or more claims of the '119 patent, including at least claim 1, under 35 U.S.C. § 271(e)(2)(C), by filing their aBLA for the express purpose of obtaining approval to engage in the commercial manufacture, use, or sale of a drug, the use of which is claimed in a patent, before the expiration of such patent.

521. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of [redacted] and/or PB006 will infringe one or more claims of the '119 patent.

522. Biogen is entitled to a judicial declaration that Defendants have infringed or will infringe, and/or are currently inducing infringement, and/or will induce infringement, directly or indirectly, literally and/or under the doctrine of equivalents, one or more claims of the '119 patent.

523. Defendants' infringement has and will continue to damage Biogen, who is entitled to recover jointly and severally from Defendants under 35 U.S.C. § 284 the damages resulting from Defendants' wrongful acts in an amount to be determined at trial, and in any event no less than a reasonably royalty.

524. Moreover, Defendants' infringement has caused, and will continue to cause, irreparable injury to Biogen, injury for which damages are an inadequate remedy unless Defendants, together with, *inter alia*, all subsidiaries, partners, co-marketers, and licensees, are enjoined from any and all activities that would infringe the claims of the '119 patent.

PRAYER FOR RELIEF

WHEREFORE, Biogen respectfully requests the following relief:

A. Judgment that Defendants have infringed and/or a declaration that Defendants will infringe one or more claims of the Asserted Patents, directly, and/or indirectly, literally and/or under the doctrine of equivalents;

B. Judgment that Defendants' infringement of one or more claims of the '641, '234, and '423 patents was willful and deliberate, an injunction, and a three-fold increase in the award of any damages in accordance with 35 U.S.C. § 284;

C. A declaration that the manufacture, use, offer for sale, sale, and/or importation of PB006 and/or [redacted] has infringed or will infringe one or more claims of the Asserted Patents;

D. A declaration that the Asserted Patents are valid and enforceable;

E. An award for an accounting of damages from Defendants' infringement;

F. A declaration that this case is exceptional pursuant to 35 U.S.C. § 285, and an award of attorneys' fees and costs pursuant to 35 U.S.C. § 285 and 35 U.S.C. § 271(e)(4);

G. Preliminary and/or permanent injunctive relief, including pursuant to 35 U.S.C. § 271(e)(4)(B) or any other relevant ground, including an order that including an order that Defendants and any of their affiliates, subsidiaries, officers, directors, employees, agents, representatives, licensees, successors, assigns, and all those acting for any of them and/or on any of their behalf, and other persons in active concert or participation with any of them directly and/or indirectly, be preliminarily and permanently enjoined from infringing, inducing others to infringe, or contributing to the infringement of the Asserted Patents; and

H. An award of such other and further relief as the Court may deem just and proper.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Karen Jacobs

Jack Blumenfeld (#1014)
Karen Jacobs (#2881)
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899-1347
(302) 658-9200
jblumenfeld@morrisnichols.com
kjacobs@morrisnichols.com

Attorneys for Plaintiffs
Biogen Inc. and Biogen MA Inc.

OF COUNSEL:

Eric J. Marandett
Anita M.C. Spieth
Greta A. Fails
Emily H. Miller
CHOATE HALL & STEWART LLP
Two International Place
Boston, MA 02110
(617) 248-5000

September 9, 2022