IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

GENENTECH, INC., HOFFMANN-LA ROCHE, INC., and CHUGAI PHARMACEUTICAL CO., LTD, Plaintiffs, v. BIOGEN MA INC and BIO-THERA SOLUTIONS, LTD., Defendants.	Case No.: _____ **JURY TRIAL DEMANDED**

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Genentech, Inc. ("Genentech") is licensed by the U.S. Food and Drug Administration ("FDA") to make and sell Actemra®, a treatment for rheumatoid arthritis and other serious inflammatory diseases. Defendant Biogen MA Inc. ("Biogen") is seeking FDA approval under the Biologics Price Competition and Innovation Act ("BPCIA"), 42 U.S.C. §§ 262(k)-(*l*), to commercialize "BIIB800," a proposed biosimilar to Genentech's drug Actemra® (tocilizumab). To vindicate their patent rights, Plaintiffs bring this Complaint seeking a judgment of patent infringement against Defendants under 35 U.S.C. § 271(e) and the BPCIA.

THE PARTIES, JURISDICTION, AND VENUE

1. Genentech is a corporation organized under the laws of the State of Delaware with its principal place of business at 1 DNA Way, South San Francisco, California 94080. The company is dedicated to discovering, developing, and commercializing medicines to treat patients with debilitating and life-threatening diseases.

2. Hoffmann-La Roche, Inc. ("HLR") is a corporation organized under the laws of the State of New Jersey with its principal place of business is 150 Clove Road, Little Falls, New

Jersey, 07424.

3. Chugai Pharmaceutical Co., Ltd ("Chugai") is a corporation organized under the laws of Japan. Chugai's principal place of business is 1-1 Nihonbashi-Muromachi 2-chome, Chuo-ku, Tokyo 103-8324 Japan.

4. For ease of reference, Genentech, HLR, and Chugai are referred to herein collectively as "Plaintiffs."

5. Biogen is a corporation organized under the laws of the Commonwealth of Massachusetts with its principal place of business is 225 Binney Street, Cambridge, Massachusetts 02142 United States.

6. Biogen develops, manufactures, distributes, sells, and/or imports drug products for the entire United States market and, on information and belief, does business in every state, including Massachusetts, either directly or indirectly.

7. On information and belief, Bio-Thera Solutions, Ltd. ("Bio-Thera") is a corporation organized and existing under the laws of China, having its corporate offices and principal place of business at Floor 5, Building A6, 11 Kai-Yuan Blvd, Huangpu District, Guangzhou, China.

8. On information and belief, Bio-Thera is in the business of, among other things, developing and manufacturing biosimilars of branded pharmaceutical drug products for marketing by others throughout the United States, including Massachusetts.

9. On information and belief, Bio-Thera manufactures BIIB800 for Biogen pursuant to the specifications provided in Biogen's biosimilar application to file a more abbreviated Biologics License Application ("aBLA") pursuant to 42 U.S.C. § 262(k) and will participate in the importation of BIIB800 into the United States. On information and belief, FDA will inspect

Bio-Thera's production facilities as part of FDA's consideration of Biogen's aBLA.

10. On information and belief, Biogen and Bio-Thera acted in concert to prepare and submit Biogen's aBLA to FDA. Bio-Thera prepared, created, approved, and/or assembled documentation in support of Biogen's aBLA. For example, several of the documents included within Biogen's aBLA indicate that they were generated by Bio-Thera and describe activities performed by Bio-Thera.

11. On information and belief, Bio-Thera actively encouraged, recommended, and/or promoted that Biogen prepare and submit Biogen's aBLA to FDA.

12. On information and belief, Biogen and Bio-Thera know and intend that upon FDA approval of Biogen's aBLA, Bio-Thera will manufacture BIIB800; and Biogen will directly or indirectly market, sell, and distribute BIIB800 throughout the United States, including in Massachusetts.

13. On information and belief, following any FDA approval of BIIB800, Biogen and Bio-Thera will act in concert to distribute and sell BIIB800 throughout the United States, including within Massachusetts.

14. For ease of reference, Biogen and Bio-Thera are referred to herein collectively as "Defendants."

15. Plaintiffs' claims for patent infringement arise under the patent laws of the United States, Title 35 of the United States Code, Title 42 of the United States Code, and the Declaratory Judgment Act, 28 U.S.C. §§ 2201-2202. This Court therefore has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

16. This Court has personal jurisdiction over Biogen because it is incorporated in Massachusetts and has its principal place of business in Massachusetts; because Biogen is

seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of BIIB800 in the United States, including in the Commonwealth of Massachusetts; and because, if its product receives FDA approval, Biogen intends to market, distribute, offer for sale, and/or sell it in the United States, including in the Commonwealth of Massachusetts, deriving substantial revenue therefrom.

17. Because Biogen has its principal place of business in this District, venue is proper under 28 U.S.C. §§ 1391 and 1400(b).

18. This Court has personal jurisdiction over Bio-Thera because, among other things, Bio-Thera, itself and in concert with Biogen, has purposefully availed itself of the benefits and protections of Massachusetts's laws such that it should reasonably anticipate being haled into court in Massachusetts. On information and belief, Bio-Thera, in concert with Biogen, is seeking approval to engage in the commercial manufacture of BIIB800 for distribution in the United States, including in Massachusetts; and because, if BIIB800 receives FDA approval, Bio-Thera will facilitate Biogen's marketing, distribution, offer for sale, and/or sale of it in the United States, including in Massachusetts, deriving substantial revenue therefrom.

19. Venue is proper in this District under 28 U.S.C. §§ 1391 and 1400(b) with respect to Bio-Thera at least because, on information and belief, Bio-Thera is a foreign corporation that may be sued in any judicial district in which it is subject to the Court's personal jurisdiction.

FACTUAL BASIS FOR RELIEF

20. The active ingredient of Actemra®, tocilizumab, is a genetically engineered antibody that inhibits the biological activity of the cytokine interleukin 6 ("IL-6"). Within the human body, IL-6 signaling can lead to chronic inflammation. Tocilizumab treats this inflammation by binding to IL-6 receptors and disrupting this biologic activity.

21. Following over a decade of research and development, Genentech filed

Biologics License Application No. 125276 with FDA with respect to Actemra®. In 2010, FDA approved Actemra® for the treatment of rheumatoid arthritis based on several Phase 3 clinical trials. Those studies demonstrated that unlike conventional therapies for RA that focused on relieving pain, Actemra® was found to inhibit progression of structural joint damage, improve the functionality of joints, as well as improve patients' pain and quality of life.

22. Since then, FDA has approved Actemra® for the treatment of several additional indications including Systemic Juvenile Idiopathic Arthritis, Polyarticular Juvenile Idiopathic Arthritis, Giant Cell Arteritis, CAR T Cell-Induced Cytokine Release Syndrome, and Systemic Sclerosis-Associated Interstitial Lung Disease. Most recently, Actemra® helped to address the COVID-19 pandemic and has been approved to treat COVID-19 in hospitalized adults.

23. The BPCIA provides for a substantially abbreviated regulatory approval pathway for biosimilars by allowing applicants rely on the extensive clinical testing previously conducted, at great expense, by the innovator company that developed the medicine the applicant wants to copy. Rather than seeking approval for the drug by filing a traditional Biologics License Application pursuant to 42 U.S.C. § 262(a), the BPCIA permits a biosimilar applicant to file an aBLA pursuant to 42 U.S.C. § 262(k).

24. In exchange for this accelerated and less expensive application process, the BPCIA obligates a biosimilar applicant to address a reference product sponsor's relevant patents in a manner that permits adjudication of patent rights before commercialization of the biosimilar product. The BPCIA does so through its so-called "patent dance."

25. The BPCIA requires (i) the biosimilar applicant to provide its aBLA as well as other information that describes the process or processes used to manufacture the biological

product that is the subject of such application to the innovator company (referred to in the statute as the "reference product sponsor," or "RPS"); (ii) the RPS to identify patents it owns or exclusively licenses that it reasonably believes the biosimilar would infringe; and (iii) both sides prior to any litigation to exchange their respective infringement and validity positions. *See* 42 U.S.C. § 262(*l*).

26. The BPCIA also requires the applicant to provide the reference product sponsor 180-days advance notice before commencing sales of any approved biosimilar. This statutory mechanism allows the RPS to file suit and seek a timely and unhurried hearing on a motion to preliminarily enjoin a product launch "until the court decides the issue of patent validity, enforcement, and infringement with respect to any patent" the RPS has identified. 42 U.S.C. § 262 (*l*)(8)(A), (B).

27. The first step in the statutory patent dance required Biogen, within 20 days of when FDA accepted its application, to supply Genentech with the aBLA for BIIB800 as well as "such other information that describes the process or processes used to manufacture the biological product that is the subject of such application." 42 U.S.C. § 262(*l*)(2)(A). Although Biogen provided Genentech with its aBLA, Biogen failed to provide "such other information." For example, Biogen failed to identify with particularity the chemicals it provides to its genetically-engineered cells when cultivating those cells to make its tocilizumab. This is precisely the type of information necessary to "describe the process or processes used to manufacture the biological product" and the type of information relevant to assessing whether Biogen infringes various patents, described further below.

28. Biogen's aBLA does make clear that Biogen itself does not directly make its tocilizumab product. Rather, Bio-Thera Solutions Ltd, a Chinese company, makes BIIB800 at

facilities in Guangzhou, China. Based on public statements regarding the contractual relationship between Biogen and Bio-Thera,[1] Bio-Thera's activities are performed on behalf of Biogen, for Biogen's benefit, and pursuant to the specifications provided in Biogen's aBLA, and thus Bio-Thera's manufacturing activities are under Biogen's direction and control. In exchange, Bio-Thera stands to receive "potential milestone payments" and "tiered royalties" if Biogen commercializes BIIB800 in the United States.

29. After receipt of Biogen's aBLA on December 12, 2022, Genentech complained to Biogen that its production excluded "other information" about the manufacturing process for BIIB800 that was necessary for Genentech to evaluate the full scope of infringement of its patents. Genentech requested that Biogen provide such information, for example, on January 23, 2023, February 1, 2023, and February 8, 2023. Biogen declined to provide the requested information. Reserving its rights for that production failure, Genentech supplied Biogen with a list of patents for which "a claim of patent infringement could reasonably be asserted" if Biogen commercialized its product. 42 U.S.C. § 262(*l*)(3)(A).

30. Upon receiving Genentech's patent lists, Biogen was required by the BPCIA to serve "detailed statements" for the patents on the original list. By statute, a biosimilar applicant's detailed statements must either represent that it will not begin commercial marketing of its biosimilar product before the patent expires (under 42 U.S.C. § 262(*l*)(3)(B)(ii)(II)) or allege that the patent is invalid or not infringed (under § 262(*l*)(3)(B)(ii)(I)). On April 11, 2023, Biogen purported to serve "detailed statements" regarding the listed patents. Biogen's statements lacked the level of factual detail required by § 262(*l*)(3)(B).

[1] For example, Biogen's press release at: https://investors.biogen.com/news-releases/news-release-details/biogen-and-bio-thera-solutions-announce-commercialization-and

31. Pursuant to § 262(*l*)(3)(C), Genentech timely provided its detailed responses to Biogen's contentions, setting forth particular grounds for infringement based on the confidential information in Biogen's aBLA and rebutting Biogen's noninfringement and invalidity allegations. Because Genentech has already served upon Biogen hundreds of pages of detailed (*l*)(3)(C) contentions setting forth and putting Biogen on notice of the factual and legal basis for the allegations made in this lawsuit, the infringement allegations set forth below do not repeat any specific content of Biogen's aBLA, which Biogen has designated as confidential under 42 U.S.C. § 262(*l*)(1)(A).

32. Pursuant to § 262(*l*)(4)(A), the parties negotiated regarding which patents on Genentech's list should be litigated in a § 271(e) infringement action. On June 27, 2023, Biogen sent Genentech a letter indicating that the parties had failed to agree upon a list of patents and selecting a number of patents as to which the parties would then be required to exchange lists pursuant to § 262(*l*)(5). The patents that were identified on one or both of the parties' lists are listed in the next section of the Complaint.

PLAINTIFFS' PATENTS

33. Biologic medicines like tocilizumab are complex. The innovative work done to develop tocilizumab has been recognized by the Patent Office with multiple patents covering various aspects of making and using the drug.

34. Because Biogen has not complied with its production obligation under 42 U.S.C. § 262(l), Genentech has been forced to assess Biogen's infringement based on incomplete information, including, but not limited to, the above-described materials it sent to and received from Biogen. Nevertheless, based on, among other things, such materials, Genentech has reason to believe that the manufacture, use, sale, or offer for sale, or importation of BIIB800 has or will infringe U.S. Patent Nos. 7,332,289; 7,521,052; 8,398,980; 8,512,983; 8,574,869; 8,734,800;

9,714,293; 9,902,777; 10,017,732; 10,336,983; 10,501,769; 10,662,237; 10,676,710; 10,744,201; 10,829,732; 10,982,003; 11,021,728; 11,078,294; 11,136,610; and 11,377,678. Copies of these patents are attached to this Complaint as Exhibits 1-20.

35. The Asserted Patents are each owned by one or more of Plaintiffs, and none of them has yet expired. To the extent that Genentech is not the owner of an Asserted Patent, it is the exclusive licensee of that patent with respect to tocilizumab with the right to enforce that patent against Biogen pursuant to a patent licensing agreement with Chugai Pharmaceutical Co., Ltd. and Hoffmann-La Roche, Inc.

FIRST CAUSE OF ACTION
(INFRINGEMENT OF THE '289 PATENT)

36. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

37. United States Patent No. 7,332,289 (the "'289 patent") (Exhibit 1), was duly and legally issued on February 19, 2008 and is unexpired.

38. The '289 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

39. Claim 1 of the '289 is exemplary. It recites:

> A method for removing contaminant DNA in an antibody-containing sample, which comprises the followings steps:
> 1) applying the antibody-containing sample to affinity chromatography on Protein A or Protein G;
> 2) eluting the antibody with an acidic aqueous solution of low conductivity having a molarity of 100 mM or less;
> 3) neutralizing the eluate from step (2) to form particles by addition of a buffer to raise the pH to 4 to 8, wherein the molarity of the neutralized eluate is 100 mM or less; and
> 4) removing the particles to thereby remove contaminant DNA from the antibody-containing sample.

40. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2),

and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least Claim 1 of the '052 patent.

41. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '289 patent is also an act of infringement of one or more claims of the '289 patent under 35 U.S.C. § 271(e)(2)(C)(i).

42. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '289 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

SECOND CAUSE OF ACTION
(INFRINGEMENT OF THE '052 PATENT)

43. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

44. United States Patent No. 7,521,052 (the "'052 patent") (Exhibit 2), was duly and legally issued on April 21, 2009 and is unexpired.

45. The '052 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

46. Claim 1 of the '052 is exemplary. It recites:

> A method for treating rheumatoid arthritis, comprising administering an effective amount of an anti-IL-6 receptor antibody (anti-IL-6R antibody) and an effective amount of methotrexate (MTX) to a patient in need thereof, wherein the anti-IL-6R antibody is a humanized PM-1 antibody.

47. Based on the information presently available to Plaintiffs, including the

confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), the method of using Biogen's tocilizumab product instructed by Biogen's proposed labeling is covered by at least claim 1.

48. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '052 patent is also an act of infringement of one or more claims of the '052 patent under 35 U.S.C. § 271(e)(2)(C)(i).

49. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '052 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

THIRD CAUSE OF ACTION
(INFRINGEMENT OF THE '980 PATENT)

50. Plaintiffs incorporate paragraph 1-35 as if set forth herein.

51. United States Patent No. 8,398,980 (the "'980 patent") (Exhibit 3), was duly and legally issued on March 19, 2013.

52. The '980 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

53. Claim 1 of the '980 is exemplary. It recites:

> An antibody subtype (1) which is a subtype of the humanized PM-1 antibody against interleukin-6 receptor (IL-6R) comprising a heavy chain that has amino acids 1-448 of the amino acid sequence set forth in SEQID NO: 1, a heavy chain that has amino acids 1-447 of the amino acid sequence set forth in SEQID NO: 1 and a C-terminal that is Pro-NH_2 and a light chain that has the amino acid sequence set forth in SEQID NO: 2.

54. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), the tocilizumab product made by Biogen and Bio-Thera is covered by at least claim 1.

55. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '980 patent is also an act of infringement of one or more claims of the '980 patent under 35 U.S.C. § 271(e)(2)(C)(i).

56. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '980 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

FOURTH CAUSE OF ACTION
(INFRINGEMENT OF THE '983 PATENT)

57. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

58. United States Patent No. 8,512,983 (the "'983 patent") (Exhibit 4), was duly and legally issued on August 20, 2013.

59. The '983 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

60. Claim 1 of the '983 is exemplary. It recites:

> A process for producing a polypeptide in a mammalian host cell expressing said polypeptide, comprising culturing the mammalian host cell in a production phase of the culture in a glutamine-free production culture medium containing asparagine, wherein the asparagine is added at a concentration in the range of 7.5 mM to 15 mM.

61. Based on the information presently available to Plaintiffs, including the

confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

62. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '983 patent is also an act of infringement of one or more claims of the '983 patent under 35 U.S.C. § 271(e)(2)(C)(i).

63. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '983 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

FIFTH CAUSE OF ACTION
(INFRINGEMENT OF THE '869 PATENT)

64. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

65. United States Patent No. 8,574,869 (the "'869 patent") (Exhibit 5), was duly and legally issued on November 5, 2013.

66. The '869 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

67. Claim 1 of the '869 is exemplary. It recites:

> A method for the prevention of the reduction of a disulfide bond in an antibody expressed in a recombinant host cell, comprising, following fermentation, sparging the pre-harvest or harvested culture fluid of said recombinant host cell with air, wherein the amount of dissolved oxygen (dO_2) in the pre-harvest or harvested culture fluid is at least 10%.

68. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

69. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '869 patent is also an act of infringement of one or more claims of the '869 patent under 35 U.S.C. § 271(e)(2)(C)(i).

70. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '869 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

SIXTH CAUSE OF ACTION
(INFRINGEMENT OF THE '800 PATENT)

71. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

72. United States Patent No. 8,734,800 (the "'800 patent") (Exhibit 6), was duly and legally issued on May 27, 2014.

73. The '800 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

74. Claim 1 of the '800 is exemplary. It recites:

> A method of inhibiting biological activity of interleukin-6 receptor (IL-6R) with an antibody subtype against IL-6R, comprising contacting the IL-6R with the antibody Subtype, wherein the

> antibody Subtype comprises a heavy chain that has amino acids 1-448 of the amino acid sequence set forth in SEQID NO: 1 in which an N-terminal glutamine (Gln) is pyroglutamylated, a heavy chain that has amino acids 1-447 of the amino acid sequence set forth in SEQID NO: 1 in which an N-terminal glutamine (Gln) is pyroglutamylated and a C-terminal that is Pro-NH_2, and a light chain that has the amino acid sequence set forth in SEQID NO: 2.

75. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), the method of using Biogen's tocilizumab product instructed by Biogen's proposed labeling is covered by at least claim 1.

76. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '800 patent is also an act of infringement of one or more claims of the '800 patent under 35 U.S.C. § 271(e)(2)(C)(i).

77. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '800 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

SEVENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '293 PATENT)

78. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

79. United States Patent No. 9,714,293 (the "'293 patent") (Exhibit 7), was duly and legally issued on July 25, 2017.

80. The '293 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

81. Claim 1 of the ’293 is exemplary. It recites:

> A process for producing a polypeptide in a host cell expressing said polypeptide, comprising culturing the host cell in a production phase of the culture in a glutamine-free production culture medium containing asparagine and aspartic acid, wherein the asparagine is added at a concentration in the range of 7.5 mM to 15 mM and wherein the aspartic acid is added at a concentration in the range of 1 mM to 10 mM.

82. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

83. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the ’293 patent is also an act of infringement of one or more claims of the ’293 patent under 35 U.S.C. § 271(e)(2)(C)(i).

84. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the ’293 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

EIGHTH CAUSE OF ACTION
(INFRINGEMENT OF THE ’777 PATENT)

85. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

86. United States Patent No. 9,902,777 (the “’777 patent”) (Exhibit 8), was duly and legally issued on February 27, 2018.

87. The ’777 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

88. Claim 1 of the ’777 is exemplary. It recites:

> A method of producing an antibody subtype 1 comprising culturing a host cell comprising at least one nucleic acid encoding for a heavy chain and at least one nucleic acid encoding for a light chain of an anti-IL-6R antibody, wherein said antibody subtype 1 comprises a heavy chain that has amino acids 1-448 of the amino acid sequence set forth in SEQ ID NO: 1, a heavy chain that has amino acids 1-447 of the amino acid sequence set forth in SEQ ID NO: 1 and a C-terminal that is Pro-NH2, and a light chain that has the amino acid sequence set forth in SEQ ID NO: 2

89. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

90. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the ’777 patent is also an act of infringement of one or more claims of the ’777 patent under 35 U.S.C. § 271(e)(2)(C)(i).

91. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the ’777 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

NINTH CAUSE OF ACTION
(INFRINGEMENT OF THE ’017,732 PATENT)

92. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

93. United States Patent No. 10,017,732 (the “’017,732 patent”) (Exhibit 9), was duly and legally issued on July 10, 2018.

94. The ’017,732 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

95. Claim 1 of the ’017,732 is exemplary. It recites:

> A method of producing a recombinant antibody composition with reduced color intensity, comprising the steps of:
>
> culturing a cell comprising a nucleic acid encoding the recombinant antibody in a cell culture medium, wherein the cell culture medium comprises one or more of components (a)-(d):
> (a) hypotaurine,
> (b) s-carboxymethylcysteine,
> (c) butylated hydroxyanisole, and
> (d) quercitrin hydrate; and
> producing the recombinant antibody;
> wherein the cell culture medium comprising one or more of components (a)-(d) reduces the color intensity of a composition comprising the recombinant antibody produced by the cell as compared to a composition comprising the recombinant antibody produced by the cell cultured in a cell culture medium that does not comprise one or more of components (a)-(d)

96. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

97. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale,

or import into the United States, of BIIB800 before the expiration of the '017,732 patent is also an act of infringement of one or more claims of the '017,732 patent under 35 U.S.C. § 271(e)(2)(C)(i).

98. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '017,732 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

TENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '983 PATENT)

99. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

100. United States Patent No. 10,336,983 (the "'983 patent") (Exhibit 10), was duly and legally issued on July 2, 2019.

101. The '983 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

102. Claim 1 of the '983 is exemplary. It recites:

> A method for increasing specific productivity (qP) of a recombinant Chinese Hamster Ovary (CHO) cell that produces an exogenous polypeptide, the method comprising culturing the CHO cell in a culture medium comprising meta-tyrosine at a concentration of from 0.2 mM to 0.7 mM, whereby the specific productivity (qP) is increased by at least 5% compared to an identical culturing process without supplementation of meta-tyrosine in the culture medium.

103. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-

Thera to make its tocilizumab biosimilar is covered by at least claim 1.

104. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '983 patent is also an act of infringement of one or more claims of the '983 patent under 35 U.S.C. § 271(e)(2)(C)(i).

105. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '983 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

ELEVENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '769 PATENT)

106. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

107. United States Patent No. 10,501,769 (the "'769 patent") (Exhibit 11), was duly and legally issued on December 10, 2019.

108. The '769 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

109. Claim 1 of the '769 is exemplary. It recites:

> A method for the production of an immunoglobulin comprising
>
> a) cultivating a Chinese Hamster Ovary (CHO) cell comprising a nucleic acid encoding the immunoglobulin in a cultivation medium with restricted glucose feeding wherein the amount of glucose available in the cultivation medium per time unit is kept constant in all time units in which restricted glucose feeding is performed and the degree of glucose limitation (DGL) is limited to a single constant value in a range between 0.5 and 0.1, wherein feeding is started once the amount of glucose present in the cultivation medium has dropped to or below a preset value in the cultivation and wherein said cultivation is a fed-batch cultivating, and

b) recovering the immunoglobulin.

110. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

111. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '769 patent is also an act of infringement of one or more claims of the '769 patent under 35 U.S.C. § 271(e)(2)(C)(i).

112. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '769 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

TWELFTH CAUSE OF ACTION
(INFRINGEMENT OF THE '237 PATENT)

113. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

114. United States Patent No. 10,662,237 (the "'237 patent") (Exhibit 12), was duly and legally issued on May 26, 2020.

115. The '237 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

116. Claim 1 of the '237 is exemplary. It recites:

> A method of virus filtration comprising subjecting a composition comprising a recombinant protein produced in a mammalian host cell and having or suspected of having a parvovirus contaminant to a virus filtration process comprising a cation exchange step and an endotoxin removal step, simultaneously or in either order, immediately preceding a virus filter capable of removing a parvovirus, and wherein said virus filter's filtration capacity in kg/m^2 is improved between 1.5 to 20 fold, as compared to no prefiltration step or using either cation exchange step or endotoxin removal step alone.

117. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

118. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '237 patent is also an act of infringement of one or more claims of the '237 patent under 35 U.S.C. § 271(e)(2)(C)(i).

119. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '237 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

THIRTEENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '710 PATENT)

120. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

121. United States Patent No. 10,676,710 (the "'710 patent") (Exhibit 13), was duly and legally issued on June 9, 2020.

122. The ’710 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

123. Claim 1 of the ’710 is exemplary. It recites:

> A method of producing a recombinant polypeptide composition with reduced color intensity, comprising the steps of:
>
> culturing a Chinese hamster ovary (CHO) cell comprising a nucleic acid encoding the recombinant polypeptide in a cell culture medium, wherein the cell culture medium comprises one or more of components (a)-(h):
>
> (a) hypotaurine,
> (b) s-carboxymethylcysteine,
> (c) camosine,
> (d) anserine,
> (e) butylated hydroxyanisole,
> (f) lipoic acid,
> (g) quercitrin hydrate, and
> (h) taurine; and
>
> producing the recombinant polypeptide;
>
> wherein the cell culture medium comprising the one or more of components (a)-(h) reduces the color intensity of the composition comprising the recombinant polypeptide produced by the cell as compared to a composition comprising the recombinant polypeptide produced by the cell cultured in a cell culture medium that does not comprise the one or more of components (a)-(h).

124. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(l)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

125. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or

import into the United States, of BIIB800 before the expiration of the '710 patent is also an act of infringement of one or more claims of the '710 patent under 35 U.S.C. § 271(e)(2)(C)(i).

126. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '710 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

FOURTEENTH OF ACTION
(INFRINGEMENT OF THE '201 PATENT)

127. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

128. United States Patent No. 10,744,201 (the "'201 patent") (Exhibit 14), was duly and legally issued on August 18, 2020.

129. The '201 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

130. Claim 1 of the '201 is exemplary. It recites:

> A method for increasing the likelihood of achieving an American College of Rheumatology (ACR) response in a rheumatoid arthritis patient compared to treating the patient with methotrexate (MTX) alone, comprising administering to the patient a combination of (i) 8 mg/kg of a humanized anti-interleukin-6 receptor (anti-IL-6R) antibody MRA every four weeks, wherein the anti-IL-6R monoclonal antibody MRA is administered intravenously, and (ii) MTX orally administered once per week at a dose in a range of 10 to 25 mg.

131. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), the method of using Biogen's tocilizumab product instructed by Biogen's proposed is covered by at least claim 1.

132. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '201 patent is also an act of infringement of one or more claims of the '201 patent under 35 U.S.C. § 271(e)(2)(C)(i).

133. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '201 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

FIFTEENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '829,732 PATENT)

134. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

135. United States Patent No. 10,829,732 (the "'829,732 patent") (Exhibit 15), was duly and legally issued on November 10, 2020.

136. The '829,732 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

137. Claim 1 of the '829,732 is exemplary. It recites:

> A method of producing a recombinant polypeptide composition with reduced color intensity, comprising the steps of:
>
> culturing a cell comprising a nucleic acid encoding the recombinant polypeptide in a cell culture medium, wherein the cell culture medium comprises aminoguanidine;
> producing the recombinant polypeptide;
> wherein the cell culture medium comprising the aminoguanidine reduces the color intensity of a composition comprising the recombinant polypeptide produced by the cell cultured in a cell culture medium that does not comprise the aminoguanidine.

138. Based on the information presently available to Plaintiffs, including the

confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

139. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '829,732 patent is also an act of infringement of one or more claims of the '829,732 patent under 35 U.S.C. § 271(e)(2)(C)(i).

140. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '829,732 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

SIXTEENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '003 PATENT)

141. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

142. United States Patent No. 10,982,003 (the "'003 patent") (Exhibit 16), was duly and legally issued on April 20, 2021.

143. The '003 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

144. Claim 1 of the '003 is exemplary. It recites:

> A process for producing an antibody in a Chinese hamster ovary (CHO) host cell expressing said antibody, comprising culturing the CHO host cell in a production phase of the culture in a glutamine-free production culture medium containing asparagine.

145. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

146. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '003 patent is also an act of infringement of one or more claims of the '003 patent under 35 U.S.C. § 271(e)(2)(C)(i).

147. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '003 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

SEVENTEENTH OF ACTION
(INFRINGEMENT OF THE '728 PATENT)

148. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

149. United States Patent No. 11,021,728 (the "'728 patent") (Exhibit 17), was duly and legally issued on June 1, 2021.

150. The '728 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

151. Claim 1 of the '728 is exemplary. It recites:

> A composition comprising Tocilizumab protein with mannose-5 glycostructure (M5) attached to Asn^{297} of the Tocilizumab protein, wherein the fraction of M5 is in a range from 2.8% to 6% of the sum

> comprising MS, G(O), G(l), and G(2) oligosaccharide attached to Asn^{297} of the Tocilizumab protein, wherein the fraction equals area % fraction deter- mined in a liquid chromatography method.

152. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the tocilizumab product made by Biogen and Bio-Thera is covered by at least claim 1.

153. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '728 patent is also an act of infringement of one or more claims of the '728 patent under 35 U.S.C. § 271(e)(2)(C)(i).

154. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '728 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

EIGHTEENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '294 PATENT)

155. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

156. United States Patent No. 11,078,294 (the "'294 patent") (Exhibit 18), was duly and legally issued on August 3, 2021.

157. The '294 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

158. Claim 1 of the '294 is exemplary. It recites:

> A method for producing an antibody, comprising expressing the antibody in a Chinese Hamster Ovary (CHO) recombinant host cell culture, and following a production phase of the cell culture, sparging the pre-harvest cell culture fluid of the recombinant host cell with air to inhibit reduction of a disulfide bond in the antibody during processing, wherein the antibody is a therapeutic monoclonal antibody, and wherein the air sparging is continued until the amount of dissolved oxygen (dO) in the pre-harvest cell culture fluid is at least 10%.

159. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs' reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

160. The submission of Biogen's aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the '294 patent is also an act of infringement of one or more claims of the '294 patent under 35 U.S.C. § 271(e)(2)(C)(i).

161. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '294 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

NINETEENTH CAUSE OF ACTION
(INFRINGEMENT OF THE '610 PATENT)

162. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

163. United States Patent No. 11,136,610 (the "'610 patent") (Exhibit 19), was duly and legally issued on October 5, 2021.

164. The ’610 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

165. Claim 1 of the ’610 is exemplary. It recites:

> A composition comprising Tocilizumab protein with mannose-5 glycostructure (MS) attached to Asn^{297} of the Tocilizumab protein, wherein area % fraction of the MS is in a range from 2.8 to 8% of the sum comprising MS, G(O), G(l), and G(2) oligosaccharide attached to Asn^{297} of the Tocilizumab protein.

166. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the tocilizumab product made by Biogen and Bio-Thera is covered by at least claim 1.

167. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the ’610 patent is also an act of infringement of one or more claims of the ’610 patent under 35 U.S.C. § 271(e)(2)(C)(i).

168. Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the ’610 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

TWENTIETH CAUSE OF ACTION
(INFRINGEMENT OF THE ’678 PATENT)

169. Plaintiffs incorporate paragraphs 1-35 as if fully set forth herein.

170. United States Patent No. 11,377,678 (the “’678 patent”) (Exhibit 20), was duly

and legally issued on July 5, 2022.

171. The ’678 patent was included on the list of patents provided by Genentech to Biogen pursuant to 42 U.S.C. § 262(*l*)(3)(A).

172. Claim 1 of the ’678 is exemplary. It recites:

> A method for production of a composition comprising Tocilizumab protein with mannose-5 glycostructure (M5) attached to Asn^{297} of the Tocilizumab protein, wherein the area % fraction of MS is in a range from 2.8 to 10% of the area sum comprising M5, G(0), G(l), and G(2) glycostructure attached to Asn^{297} of the Tocilizumab protein, wherein the area % fraction is determined by a method comprising liquid chromatography, comprising:
>
> a. cultivating recombinant Chinese Hamster Ovary (CHO) cells comprising one or more nucleic acids encoding the Tocilizumab protein in a cultivation medium under continuous or fed-batch cultivation conditions to produce the composition, wherein initial CHO cell density comprises at least 10^5 cells/ml and a pH set-point of the cultivation is between 7.0 and 7.2, and an amount of glucose available in the cultivation medium is in a range from 80% to 10% of the amount that could maximally be utilized by the CHO cells in the cultivation medium; and
>
> b. recovering the composition from the cultivation medium.

173. Based on the information presently available to Plaintiffs, including the confidential information disclosed to Genentech by Biogen pursuant to 42 U.S.C. § 262(*l*)(2), and on Plaintiffs’ reasonable belief with respect to matters as to which Biogen has elected not to disclose information about its processes, the manufacturing process used by Biogen and Bio-Thera to make its tocilizumab biosimilar is covered by at least claim 1.

174. The submission of Biogen’s aBLA by Biogen in concert with Bio-Thera to obtain FDA approval to engage in the commercial manufacture, use, offer for sale, and/or sale, or import into the United States, of BIIB800 before the expiration of the ’678 patent is also an act of infringement of one or more claims of the ’678 patent under 35 U.S.C.

§ 271(e)(2)(C)(i).Genentech will be irreparably harmed if Defendants are not enjoined from infringing one or more claims of the '678 patent. Genentech has no adequate remedy at law. Genentech is entitled to injunctive relief at least under 35 U.S.C. § 271(e)(4)(B) and § 271(e)(4)(D) preventing Defendants from any further infringement, damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C), and fees under 35 U.S.C. § 271(e)(4) and § 285.

PRAYER FOR RELIEF

WHEREFORE, Genentech requests the following relief:

(a) A judgment that Defendants infringed the Asserted Patents by filing their aBLA because it will infringe the Asserted Patents if Biogen were to commercialize BIIB800 in the United States;

(b) Statutory relief under 35 U.S.C. § 271(e)(4)(D), including but not limited to a permanent injunction prohibiting Defendants, their officers, partners, agents, servants, employees, parents, subsidiaries, affiliate corporations, other related business entities, and all other persons acting in concert, participation, or in privity with them and/or their successors or assigns from infringing the patents in suit, or contributing to the same, or actively inducing anyone to do the same, by acts including the manufacture, use, offer to sell, sale, distribution, or importation of any current or future versions of a product that infringes, or the use or manufacturing of which infringes, the patents in suit;

(c) Damages pursuant to 35 U.S.C. § 271(e)(4)(C), if applicable, in the form of lost profits but in no event less than a reasonable royalty;

(d) A judgment that the infringement has been willful and an enhancement of damages;

(e) An award for an accounting of any damages from Defendants' infringement;

(f) Preliminary and/or permanent equitable relief, including pursuant to 35 U.S.C. § 271(e)(4)(B), including but not limited to a preliminary and permanent injunction that enjoins

Defendants, their officers, partners, agents, servants, employees, parents, subsidiaries, affiliate corporations, other related business entities, and all other persons acting in concert, participation, or in privity with them and/or their successors or assigns from infringing the patents in suit, or contributing to the same, or actively inducing anyone to do the same, by acts including the manufacture, use, offer to sell, sale, distribution, or importation of any current or future versions of a product that infringes, or the use or manufacturing of which infringes, the patents in suit;

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

(h) An award of Plaintiffs' costs and expenses in this action; and

(i) Such further relief as this court may deem just and proper.

JURY DEMAND

Pursuant to Rule 38 of the Federal Rules of Civil Procedure, Plaintiffs hereby demand trial by jury of all issues so triable by a jury in this action.

Date: July 13, 2023

Of Counsel:

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