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Attorneys for Plaintiff
GENZYME CORPORATION

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

GENZYME CORPORATION,

Plaintiff,

vs.

GENENTECH, INC. and CITY OF HOPE,

Defendants.

Case No. 2:15-cv-09991

COMPLAINT FOR DECLARATORY JUDGMENT OF INVALIDITY AND NON-INFRINGEMENT

DEMAND FOR JURY TRIAL

Plaintiff Genzyme Corporation ("Genzyme"), for its Complaint against Genentech, Inc. ("Genentech") and City of Hope (collectively, "Defendants"), allege as follows:

NATURE OF THE CASE

1. Genzyme seeks a declaration that U.S. Patent No. 7,923,221 titled "Methods of Making Antibody Heavy and Light Chains Having Specificity for a Desired Antigen" (the "Cabilly III patent," attached as Exhibit A) is invalid and not infringed by the manufacture, use, sale, offer to sale, or importation of Genzyme's Lemtrada® (alemtuzumab) antibody product. The Cabilly III patent was filed on April 13, 1995, and issued on April 12, 2011.

2. The Cabilly III patent is a continuation of U.S. Patent No. 6,331,415 titled "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein" (the "Cabilly II patent"). The Cabilly II patent is a continuation of U.S. Patent No. 4,816,567 (the "Cabilly I patent"), which was filed on April 8, 1983 and expired on March 28, 2006. (The Cabilly I, II and III patents will collectively be referred to as the "Cabilly patents"). The Cabilly I and II patents are not at issue in this case.

3. Genzyme received approval from the U.S. Food and Drug Administration ("FDA") on November 14, 2014 to market and sell the therapeutic antibody Lemtrada® (alemtuzumab) in the United States for the treatment of certain patients with relapsing forms of multiple sclerosis ("MS"), and sells Lemtrada® in the U.S. for this indication.

4. Genzyme brings this action to lift the cloud created by the substantial, immediate and real controversy between the parties in light of Genzyme's contention that Genzyme has the right to manufacture, use, sell, offer to sell and import Lemtrada® without a license under any of the Cabilly patents, including the Cabilly III patent. Without declaratory relief, the substantial, immediate and real controversy between the parties poses a substantial risk of injury to Genzyme, as well as to the patients using Lemtrada® and the doctors and nurses using Lemtrada® to treat them. The continued existence and threat of enforcement of this invalid

patent impedes the manufacturing, marketing, sale, importation and use of Lemtrada®.

5. Defendants have contended that the Cabilly patents broadly cover the use of certain well-known, conventional recombinant methods to produce any antibody product in any type of host cell. Defendants have filed infringement claims asserting the Cabilly patents against numerous companies who have made and sold antibody products produced using recombinant methods allegedly similar to the recombinant methods Genzyme uses to make Lemtrada®. On information and belief, Genentech is also developing its own antibody product (ocrelizumab) for the treatment of relapsing MS, which is set for FDA submission in early 2016. Press Release, Genentech, "Genentech's Ocrelizumab First Investigational Medicine to Show Efficacy in People with Primary Progressive Multiple Sclerosis in Large Phase III Study" (Sept. 27, 2015) (attached as Exhibit B). Defendants have made public statements about pursuing an aggressive litigation policy to protect its products against competition and to protect against alleged infringement of the Cabilly patents.

6. Given Defendants' past acts and statements, and Genzyme's sales of Lemtrada® in the United States, a real, immediate, and substantial dispute exists between the parties concerning the Cabilly III patent, for which Genzyme seeks declaratory relief.

THE PARTIES

7. Plaintiff Genzyme Corporation is a Massachusetts corporation with a principal place of business at 500 Kendall Street, Cambridge, Massachusetts 02142.

8. On information and belief, Defendant Genentech, Inc. is a Delaware corporation with its principal place of business at 1 DNA Way, South San Francisco, California 94080. On information and belief, Genentech conducts business in this District.

9. On information and belief, Defendant City of Hope is a California not-for-profit organization with its principal place of business in at 1500 East Duarte Road, Duarte, California 91010.

10. On information and belief, Genentech and City of Hope are co-assignees of the Cabilly III patent.

JURISDICTION AND VENUE

11. This action arises under the Declaratory Judgment Act of 1934 (28 U.S.C. §§ 2201-2202), Title 28 of the United States Code, for the purposes of determining an actual and justiciable controversy between the parties, and the patent laws of the United States, Title 35 of the United States Code. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

12. This Court has personal jurisdiction over Genentech based on its principal place of business in California. This Court has personal jurisdiction over City of Hope based on its organization under the laws of the State of California and its principal place of business in this judicial district in California.

13. Venue is proper in this District pursuant to 28 U.S.C. § 1391 because City of Hope resides in this District, Genentech conducts business in this District, and a substantial part of the events or omissions giving rise to the claims occurred in this District.

INTRADISTRICT ASSIGNMENT

14. A substantial part of the events or omissions giving rise to the claims occurred in the Western Division.

GENZYME'S LEMTRADA® (ALEMTUZUMAB) PRODUCT

15. Lemtrada® (alemtuzumab) is a recombinant humanized IgG1 kappa monoclonal antibody that was genetically engineered using technology to "humanize" the antibody that was developed many years after April 8, 1983, the earliest effective filing date of the Cabilly III patent. Lemtrada® targets CD52, a protein located on the surface of immune cells, and is FDA-approved for treating

relapsing MS in certain patients. MS is a chronic inflammatory disease of the central nervous system that disrupts the communication between the brain, spinal cord, and other areas of the body, which can result in irreversible nerve deterioration and debilitation. The National Multiple Sclerosis Society estimates that approximately 400,000 Americans currently suffer from MS. Lemtrada® is particularly revolutionary for MS patients who did not respond to first- and second-line therapies. Edward Fox, M.D., Ph.D., Director of the Multiple Sclerosis Center of Central Texas, has said about the FDA approval of Lemtrada®: "It is a great day for people living with relapsing forms of MS in the United States" since "[t]he unmet need in MS remains high." Loretta Fala, *Lemtrada (Alemtuzumab) a New Treatment Option Approved by the FDA for the Treatment of Relapsing Forms of Multiple Sclerosis*, American Health & Drug Benefits (Aug. 03, 2015) (attached as Exhibit C).

16. Originally, ILEX Oncology, Inc. ("ILEX") co-developed alemtuzumab in the late 1990's with Millennium Pharmaceuticals, Inc. ("Millennium") as a treatment for chronic lymphocytic leukemia, under the trade name Campath®. ILEX and Millennium received FDA approval on May 7, 2001 to market Campath® (alemtuzumab) in the United States for the treatment of patients with B-cell chronic lymphocytic leukemia and who had been treated with alkylating agents and failed fludarabine therapy.

17. Genzyme conducted new clinical trials on alemtuzumab for MS treatment in collaboration with Bayer, and ultimately received FDA approval on November 14, 2014 to market alemtuzumab under the name "Lemtrada" in the United States for treating certain patients with relapsing forms of MS. Genzyme began to commercialize Lemtrada® immediately thereafter.

18. On March 31, 2003, ILEX entered into a non-exclusive license to the Cabilly patents with Genentech regarding Campath® (alemtuzumab) ("the Cabilly

license"). As a result of Genzyme's acquisition of ILEX in 2004, Genzyme became a licensee to the Cabilly patents with respect to sales of alemtuzumab.

19. Genzyme has expended substantial revenues researching, developing, launching and commercializing Lemtrada®. Furthermore, Genzyme has paid, and Genentech has accepted, royalties under the Cabilly patents on sales of alemtuzumab as both Campath® and Lemtrada®. On September 4, 2012, Genzyme discontinued commercialization of Campath® and no longer sells Campath® in the United States. As a result, Genzyme does not pay Genentech any licensing fees under the Cabilly patents for Campath®.

20. Genzyme believes that it owes no royalties to Defendants for Lemtrada® under the Cabilly Patents, based, in part, on Genzyme's belief that the Cabilly III patent is invalid, unenforceable, and/or not infringed by the manufacturing, sale, importation, use, or marketing of Lemtrada®.

THE CABILLY PATENTS

21. On April 8, 1983, Shmuel Cabilly, Herbert Heyneker, William Holmes, Arthur Riggs, and Ronald Wetzel (the "Cabilly Applicants") filed a patent application in the United States Patent and Trademark Office ("PTO") that issued on March 28, 1989 as the Cabilly I patent. The Cabilly Applicants assigned their rights to Genentech and the City of Hope. The Cabilly I patent expired on March 28, 2006 – almost ten years ago.

22. At the time the Cabilly I patent issued, the Cabilly Applicants had a continuation patent application pending in the PTO, which ultimately issued as the Cabilly II patent. The Cabilly II patent application copied claims from a then-existing patent, U.S. Patent No. 4,816,397 (the "Boss patent") to provoke the PTO Board of Patent Appeals and Interferences (the "PTO Board") to declare an interference proceeding to determine whether the Boss patentees or the Cabilly Applicants were entitled to priority for the invention claimed in the Boss patent.

23. In February 1991, the PTO Board declared a patent interference

between the pending Cabilly II patent application and the Boss patent on the ground that both the Boss patentees and the Cabilly Applicants claimed the same purported invention. After seven years of adversarial proceedings, in August of 1998 the PTO Board ruled the Boss patentees were entitled to priority over the Cabilly II Applicants. *See Cabilly v. Boss*, 55 U.S.P.Q.2d 1238 (B.P.A.I. 1998). The PTO Board concluded that the Cabilly Applicants had failed to establish conception or reduction to practice of the claimed inventions prior to the March 25, 1983 filing date of the Boss patent. According to the PTO Board, "there is no evidence that immunoglobulins, multiple chain proteins, had been produced by recombinant DNA techniques from a single host cell prior to March 25, 1983." Moreover, "the evidence indicates that Cabilly et al. had but a hope or wish to produce active antibodies in bacteria; and, there is no supporting evidence to establish the development of the means to accomplish that result or evidence of a disclosure to a third party of complete conception." The Final Decision therefore concluded that the Cabilly Applicants were "not entitled to a patent."

24. In October 1998, Genentech filed an action in the Northern District of California under 35 U.S.C. § 146 against the owner of the Boss patent, Celltech Therapeutics Ltd. ("Celltech"), to appeal the decision of the PTO Board awarding priority to the Boss patentees. *Genentech, Inc. v. Celltech Therapeutics Ltd.*, Case No. C98-3926 (N.D. Cal.). In March 2001, the parties to that action filed a notice of settlement and joint request for the entry of settlement instruments. As part of their settlement agreement, the parties asked the district court to find that, contrary to the PTO Board's prior decision, Genentech's Cabilly Applicants were entitled to priority. On information and belief, as part of the Genentech-Celltech agreement, Celltech obtained certain rights relating to the Cabilly II patent as well as substantial payments from Genentech in exchange for its agreement to stipulate that the Cabilly Applicants were entitled to priority for the inventions claimed in the Boss patent. The precise terms of the settlement agreement are confidential and,

despite reasonable inquiry, unknown to Genzyme.

25. Pursuant to the Genentech-Celltech agreement, the district court issued an order directing the PTO to vacate its determination that the Boss applicants were entitled to priority, to revoke the Boss patent, and to issue a patent to the Cabilly Applicants claiming the same subject matter as the Boss patent. The Cabilly II patent issued on December 18, 2001. The Cabilly II patent is assigned on its face to Genentech, and by a certificate of correction to City of Hope. The Cabilly II patent expires on December 18, 2018. The subsequently-issued Cabilly III patent is subject to a terminal disclaimer over the Cabilly II patent, and hence also expires on December 18, 2018.

26. If the PTO Board's decision in favor of the Boss patent had not been reversed as a result of the private Genentech-Celltech agreement, the Boss patent would have expired in 2006, and the public would thereafter have been free to use the inventions claimed in the Cabilly patents, as is the case everywhere in the world, except the United States. Instead, because Genentech and Celltech agreed to request that the Court reverse that result, the Defendants received the Cabilly II and Cabilly III patents, which would not be in force but for the private Genentech-Celltech agreement. Consequently, Defendants have ostensibly extended their power to exclude others from making, using, or selling the inventions claimed in the Boss Cabilly patents until 2018 — more than 35 years after the initial Cabilly I application, and more than 12 years after the prior Boss patent would have expired. The combined period of patent exclusivity secured by the Defendants for the Cabilly patents, which all share the same specification, is 29 years.

GENZYME'S DISPUTE WITH GENENTECH REGARDING THE CABILLY III PATENT

27. Genentech has aggressively enforced the Cabilly patents across the biopharmaceutical industry through multiple litigations and licensing demands.

28. Through its statements and actions, Genentech has made clear to the

biopharmaceutical industry generally, and to Genzyme specifically, that Genentech intends to enforce the Cabilly patents and contends the claims of the Cabilly patents effectively preclude others from commercially manufacturing recombinant monoclonal antibodies without Genentech's permission. In 2002, after the Cabilly II patent issued, Sean Johnston, then Genentech's Vice President of Intellectual Property and now Genentech's Senior Vice President and General Counsel said:

> "The recently issued patent **broadly covers** the coexpression of immunoglobulin heavy and light chain genes in a single host cell ... We do not believe that the claims are limited by type of antibody (murine, **humanized** [90% human sequence], or human) or by host cell type."

("Genentech Awarded Critical Antibody Patent," *Nature Biotechnology*, vol. 20, p. 108 (Feb. 2002) (emphasis added).). See Exhibit D.

29. Genentech has procured substantial royalties through licensing the Cabilly patents to "many biotechnology and pharmaceutical companies[…] for their commercial products," explaining that the patents cover "methods used to make antibodies and antibody fragments by recombinant DNA technology, as well as recombinant cells and DNA that are used in those methods." Press Release, Genentech Inc., Genentech Receives Final Notification Upholding Cabilly Patent in Reexamination Proceeding (Feb. 24, 2009) (attached as Exhibit E).

30. On information and belief, Genentech contends that the process and certain starting materials used to produce Lemtrada® (alemtuzumab) infringe one or more claims of the Cabilly III patent. Lemtrada® is made by recombinant DNA techniques, and Genentech has asserted the Cabilly patents against several other antibodies made by recombinant DNA techniques.

31. Genentech has alleged infringement of the Cabilly III patent by other manufacturers of recombinant monoclonal antibodies, including Bristol-Myers Squibb Company ("BMS"), Eli Lilly and Company ("Eli Lilly"), GlaxoSmithKline

LLC ("GSK"), Sanofi-Aventis U.S. LLC ("Sanofi") and Regeneron Pharmaceuticals, Inc. ("Regeneron"). *Eli Lilly & Co. v. Genentech, Inc.*, Civil Action No. 13-cv-0919 (N.D. Cal. 2013); *Bristol-Myers Squibb Co. v. Genentech, Inc.*, Civil Action No. 13-cv-2045 (N.D. Cal. 2013); *Glaxo Group Ltd. et al. v. Genentech, Inc. and City of Hope*, Civil Action No.10-cv-02764 (MRP)(FMO) (C.D. Cal. 2010); *Sanofi-Aventis US LLC, et al. v. Genentech, et al.* Civil Action No. 15-cv-5685 (GW)(AGR) (C.D. Cal. 2015). In fact, Genentech and City of Hope filed a patent infringement action against GSK for infringement of the Cabilly III patent on the very day that the PTO issued the Cabilly III patent. *Genentech, Inc. v. Glaxo Group Ltd.*, Civ. Act. No. 11-cv-03065 (MRP) (JEM), Docket Item No. 1 (filed April 12, 2011). In addition, Genentech has never disputed that an actual case or controversy exists whenever a company has sought a declaratory judgment of invalidity or non-infringement of the Cabilly III patent. On information and belief, Genentech contends that the recombinant methods used by Genzyme to produce Lemtrada® (alemtuzumab) are similar in relevant aspects to the recombinant methods used by BMS, Eli Lilly, GSK and Sanofi/Regeneron to produce their monoclonal antibody products: Yervoy®, Erbitux®, Benlysta®, Arzerra®, and Praluent®.

32. Genentech has also asserted the Cabilly II patent in litigation against other manufacturers of recombinant monoclonal antibodies, including MedImmune, Inc. ("MedImmune"), Centocor Ortho Biotech Inc. ("Centocor"), BMS, GSK and Eli Lilly. *MedImmune, Inc. v. Genentech, Inc.*, No. 03-02567 (MRP) (C.D. Cal. 2003); *Centocor, Inc. v. Genentech, Inc.*, No. 08-CV-3573 (MRP) (C.D. Cal. 2008). On information and belief, Genentech contends that the recombinant methods used by Plaintiffs to produce Lemtrada® (alemtuzumab) are similar in relevant aspects to the recombinant methods used by MedImmune, Centocor, GSK, BMS and Eli Lilly to produce their monoclonal antibody products: Synagis®, ReoPro®, Remicade®, Benlysta®, Arzerra®, Yervoy® and Erbitux®.

33. Genentech has made public statements about pursuing an aggressive litigation policy to protect its products against competition and to protect against alleged infringement of the Cabilly II patent claims. In its 2009 Form 10-K filing with the Securities and Exchange Commission, Genentech stated:

> "Intellectual property protection of our products is crucial to our business. Loss of effective intellectual property protection could result in lost sales to competing products and loss of royalty payments (for example, royalty income associated with the **Cabilly patent)** from licenses. We are often involved in disputes over contracts and intellectual property, and we work to resolve these disputes in confidential negotiations or litigation. We expect legal challenges in this area to continue. We plan to continue to build upon and defend our intellectual property position." (emphasis added)

Genentech also states therein: "We have in the past been, are currently, **and may in the future be involved in material litigation** and other legal proceedings related to our proprietary rights, **such as the Cabilly patent litigation and reexamination** ...." (emphasis added) (attached as Exhibit F).

34. On information and belief, Genentech has received a material amount of revenue from licensing the Cabilly patents, including from Genzyme. On information and belief, between 1991 and 2007, Genentech entered into at least 35 licenses granting rights to the Cabilly I and/or II patents. *See* Reexamination of U.S. Patent No. 6,331,415, Declaration of Dr. E. Fintan Walton Under 37 C.F.R. § 1.132, ¶25 (June 4, 2008) (attached as Exhibit G).

35. Genentech's statements that it will enforce its intellectual property, and specifically the Cabilly patents, to defend its license royalty stream, and the numerous examples of similar infringement suits it has filed, establish that a real

and immediate dispute exists between parties with adverse legal interests concerning the Cabilly III patent and Genzyme's sale of Lemtrada® (alemtuzumab) sufficient to warrant the issuance of a declaratory judgment.

FIRST CAUSE OF ACTION

PATENT INVALIDITY

36. Genzyme incorporates the allegations of paragraphs 1 through 33 as if fully set forth herein.

37. An actual and substantial controversy has arisen and now exists between the parties concerning the validity of the Cabilly III patent.

38. The Cabilly III patent is invalid because it is anticipated and/or obvious under 35 U.S.C. §§ 102 and 103.

39. The Cabilly III patent is invalid based on the judicially created doctrine of obviousness-type double patenting and/or under 35 U.S.C. §§ 101 and/or 103 in view of the expired Cabilly I patent.

40. The Cabilly III patent is invalid under 35 U.S.C. § 112 for failing to show that the inventors possessed the full scope of their claimed inventions or provided a sufficient disclosure that would allow a person of ordinary skill in the art to practice the full scope of the claims without undue experimentation.

41. Genzyme seeks a declaratory judgment that the Cabilly III patent is invalid under 35 U.S.C. §§ 101, 102, 103 and 112 (2006) and/or under the judicially created doctrine of obviousness-type double patenting.

SECOND CAUSE OF ACTION

NON-INFRINGEMENT

42. Genzyme incorporates the allegations of paragraphs 1 through 40 as fully set forth herein.

43. An actual controversy has arisen and now exists between the parties concerning whether Genzyme's manufacture, use, importation, offer for sale, or sale of Lemtrada® infringes any valid and enforceable claim of the Cabilly III

patent.

44. Genzyme seeks a declaratory judgment that making, using, importing, offering to sell, and selling Lemtrada® does not and will not infringe any valid and enforceable claim of the Cabilly III patent.

THIRD CAUSE OF ACTION

GENZYME OWES NO ROYALTIES

45. Genzyme incorporates the allegations of paragraphs 1 through 43 as fully set forth herein.

46. An actual controversy has arisen and now exists between the parties concerning whether Genzyme has any obligation to continue to pay royalties to Defendants if the Cabilly III patent is deemed to be invalid, unenforceable or not infringed.

47. Genzyme seeks a declaratory judgment that if the Cabilly III patent is declared to be invalid, unenforceable or not infringed, Genzyme is entitled to a judgment that it owes no royalties to Genentech and/or City of Hope.

PRAYER FOR RELIEF

WHEREFORE, Genzyme requests that judgment be entered in favor of Genzyme and against Genentech and City of Hope:

a) Declaring the Cabilly III patent invalid;

b) Declaring that the manufacture, use, sale, offer of sale, or importation of Genzyme's Lemtrada® product does not infringe any valid and enforceable claim of the Cabilly III patent;

c) Enjoining Genentech and City of Hope from enforcing the Cabilly III patent against Genzyme;

d) Awarding Genzyme its costs and attorney's fees; and

f) Awarding Genzyme such other relief as the Court deems just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Genzyme demands a trial by jury of all issues so triable.

Dated: December 30, 2015

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