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SANOFI-AVENTIS U.S. LLC and REGENERON PHARMACEUTICALS, INC.

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

SANOFI-AVENTIS U.S. LLC and REGENERON PHARMACEUTICALS, INC., Plaintiffs, vs. GENENTECH, INC. and CITY OF HOPE, Defendants.	Case No. 2:15-cv-05685 **COMPLAINT FOR DECLARATORY JUDGMENT OF INVALIDITY AND NONINFRINGEMENT** **DEMAND FOR JURY TRIAL**

Plaintiffs sanofi-aventis U.S. LLC ("Sanofi") and Regeneron Pharmaceuticals, Inc. ("Regeneron") (collectively, "Plaintiffs"), for their Complaint against Genentech, Inc. ("Genentech") and City of Hope (collectively, "Defendants"), allege as follows:

NATURE OF THE CASE

1. Plaintiffs seek 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 therefore not infringed by the manufacture, use, sale, offer of sale, or importation of Plaintiffs' Praluent® (alirocumab) 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") (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. Plaintiffs have received approval from the U.S. Food and Drug Administration ("FDA") to market and sell Praluent® (alirocumab) in the United States. The approved indication is for the treatment of adult patients with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-cholesterol. Plaintiffs bring this action to lift the cloud created by the imminent threat of a lawsuit by Defendants against Plaintiffs for infringement of the Cabilly III patent. Without declaratory relief, the threat of suit poses a substantial risk of injury to Plaintiffs as well as to the patients who will use Praluent® (alirocumab) and the nurses and doctors who will use Praluent® (alirocumab) in treating patients. The continued existence and threat of suit of this invalid patent impedes the manufacture, marketing and sale of Praluent® (alirocumab).

4. Defendants have asserted 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 under

the Cabilly patents against numerous companies who have made and sold antibody products that were produced using recombinant methods similar to the recombinant methods used by Plaintiffs to make Praluent® (alirocumab). Given Defendants' past acts and statements and Plaintiffs' sales of Praluent® (alirocumab) in the United States, a real, immediate, and substantial dispute exists between the parties concerning the Cabilly III patent for which Plaintiffs now seek declaratory relief.

THE PARTIES

5. Plaintiff sanofi-aventis U.S. LLC is a Delaware limited liability company having a principal place of business at 55 Corporate Drive, Bridgewater, NJ 08807.

6. Plaintiff Regeneron Pharmaceuticals, Inc. is a New York corporation having its principal place of business at 777 Old Saw Mill River Road, Tarrytown, New York 10591.

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

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

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

JURISDICTION AND VENUE

10. 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) (2006).

11. 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 because its principal place of operation is in California.

12. Venue is proper in this District pursuant to 28 U.S.C. § 1391 (2006) 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

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

PLAINTIFFS' PRALUENT® (ALIROCUMAB) PRODUCT

14. Since 2007, Sanofi and Regeneron have collaborated to discover, develop, manufacture and commercialize therapeutic monoclonal antibodies. One of these antibodies is alirocumab. Praluent® (alirocumab) is a new monoclonal antibody which targets PCSK9 (proprotein convertase subtilisin/kexin type 9), an enzyme encoded by the PCSK9 gene that acts in cholesterol homeostasis. Praluent® (alirocumab) is made by recombinant DNA techniques.

15. On July 24, 2015, Plaintiffs received approval from the FDA to market Praluent® (alirocumab) in the United States for treating adult patients with heterozygous familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-cholesterol. Praluent® (alirocumab) is the first monoclonal antibody targeting PCSK9 in the United States. On July 25, 2015, Plaintiffs began to commercialize Praluent® in the United States by offering Praluent® for sale, selling Praluent® and filling orders for Praluent®.

THE CABILLY PATENTS

16. 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 in March 2006 – over 9 years ago.

17. At the time the Cabilly I patent issued, the Cabilly Applicants had a continuation application (the "Cabilly II application") pending in the PTO. The Cabilly Applicants copied claims from U.S. Patent 4,816,397 (the "Boss patent") in order to provoke the PTO Board of Patent Appeals and Interferences to initiate an interference proceeding to determine whether the Boss patentees or the Cabilly Applicants were entitled to priority for the inventions claimed in the Boss patent.

18. In February 1991, the PTO Board declared a patent interference between the pending Cabilly II 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 the PTO, in August 1998, the PTO Board found that the Boss patentees were entitled to priority over the Cabilly 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." (emphasis added). The Final Decision therefore indicated that the Cabilly Applicants were "not entitled to a patent."

19. In October 1998, Genentech filed an action in this District 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 patent. *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 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 certain 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 Plaintiffs.

20. 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, and on its face is assigned to Genentech, and, by certificate of correction, is also assigned to City of Hope. The Cabilly II patent expires on December 18, 2018. Because the Cabilly III patent is subject to a terminal disclaimer over Cabilly II, it also expires on December 18, 2018.

21. 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 II patent, as is the case everywhere else in the world except the United States. Instead, because Genentech and Celltech agreed to request that the court reverse that result, Defendants received the Cabilly II patent, which will not expire until 2018. Consequently, due to the private Genentech-

Celltech agreement, Defendants have ostensibly extended their power to exclude others from making, using, or selling the inventions claimed in the Boss and Cabilly II patent until 2018—more than 35 years after their original 1983 patent application, and more than 12 years after the prior Boss patent would have expired. The combined period of patent exclusivity secured by Defendants for the Cabilly I, Cabilly II and Cabilly III patents, which share the same patent specification, is 29 years.

PLAINTIFFS' DISPUTE WITH GENENTECH REGARDING THE CABILLY III PATENT

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

23. Through its statements and actions, Genentech has made clear to the biopharmaceutical industry generally and to Plaintiffs that it contends that 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 co-expression 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 B.

24. Following reexamination of the Cabilly II patent in the PTO, Genentech touted the licensing of the Cabilly II patent by "many biotechnology and

pharmaceutical companies… for their commercial products," explaining that the patent broadly relates to "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." ("Genentech Receives Final Notification Upholding Cabilly Patent in Reexamination Proceeding," Genentech Press Release (Feb. 24, 2009).). See Exhibit C.

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

26. Genentech has alleged infringement of the Cabilly III patent in litigation against other manufacturers of recombinant monoclonal antibodies, including Bristol-Myers Squibb Company (“BMS”), Eli Lilly and Company (“Eli Lilly”) and GlaxoSmithKline LLC (“GSK”). 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 the USPTO issued the Cabilly III patent. In addition, Genentech has never disputed that an actual case or controversy exists whenever a company has sought a declaratory judgment of invalidity of Cabilly III. On information and belief, the recombinant methods used by Plaintiffs to produce Praluent® (alirocumab) are similar, in relevant aspects, to the recombinant methods used by BMS, Eli Lilly and GSK to produce their monoclonal antibody products Yervoy®, Erbitux®, and Benlysta® and Arzerra®.

27. Genentech has 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. On information and belief, the recombinant methods used by Plaintiffs to produce Praluent® (alirocumab) 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®, Yervoy®, Benlysta®, Arzerra® and Erbitux®.

28. 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 states:

> "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: "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)

29. On information and belief, Genentech has received a material amount of revenue from licensing the Cabilly patents. On information and belief, between 1991-2007, 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). See Exhibit D.

30. Genentech's statements that it will enforce its intellectual property,

specifically the Cabilly patents, to defend its license royalty stream establish that a real and immediate dispute exists between parties with adverse legal interests concerning the Cabilly III patent and Plaintiffs' imminent release of Praluent® (alirocumab). Plaintiffs therefore have a reasonable apprehension of suit by Genentech regarding the Cabilly III patent.

FIRST CAUSE OF ACTION

PATENT INVALIDITY

31. Plaintiffs incorporate the allegations of paragraphs 1 through 30 as fully set forth herein.

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

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

34. 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.

35. 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.

36. Plaintiffs seek 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

37. Plaintiffs incorporate the allegations of paragraphs 1 through 36 as fully set forth herein.

38. An actual controversy has arisen and now exists between the parties

concerning whether Plaintiffs' manufacture, use, importation, offer for sale, or sale of Praluent® (alirocumab) infringes any valid and enforceable claim of the Cabilly III patent.

39. Plaintiffs seek a declaratory judgment that making, using, importing, offering to sell, and selling Praluent® (alirocumab) does not and will not infringe any valid and enforceable claim of the Cabilly III patent.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs request that judgment be entered in favor of Plaintiffs and against Genentech and City of Hope:

1. Declaring the Cabilly III patent invalid;

2. Declaring that the manufacture, use, sale, offer of sale, or importation of Plaintiffs' Praluent® (alirocumab) product does not infringe any valid and enforceable claim of the Cabilly III patent;

3. Enjoining Genentech and City of Hope from enforcing the Cabilly III patent;

4. Awarding Plaintiffs their costs and attorney's fees; and

5. Awarding Plaintiffs 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, Plaintiffs demand a trial by jury of all issues so triable.

Dated: July 27, 2015

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