IN THE UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

SANOFI-AVENTIS U.S. LLC; GENZYME CORPORATION; AND REGENERON PHARMACEUTICALS, INC., **Plaintiffs,** **v.** **AMGEN INC. AND IMMUNEX CORPORATION,** **Defendants.**	**Civil Action No. _____** **DEMAND FOR JURY TRIAL**

COMPLAINT FOR DECLARATORY JUDGMENT OF NON-INFRINGEMENT

Sanofi-Aventis U.S. LLC and Genzyme Corporation (collectively, "Sanofi"), and Regeneron Pharmaceuticals, Inc. ("Regeneron"), by and through their undersigned attorneys, upon knowledge with respect to their own actions and on information and belief as to other matters, for their complaint aver as follows:

Nature of the Action

1. This is an action seeking a declaration that Sanofi and Regeneron's development, manufacturing, sale, promotion, and related activities for their product Dupixent® (dupilumab) do not directly or indirectly infringe U.S. Patent No. 8,679,487 (the "'487 Patent").

Parties

2. Plaintiff Sanofi-Aventis U.S. LLC is a limited liability company organized and existing under the laws of the State of Delaware with its principal place of business located at 55 Corporate Drive, Bridgewater, New Jersey.

3. Plaintiff Genzyme Corporation is a corporation organized and existing under the laws of the Commonwealth of Massachusetts with its principal place of business located at 500 Kendall Street, Cambridge, Massachusetts.

4. Plaintiff Regeneron is a corporation organized and existing under the laws of the State of New York with its principal place of business located at 777 Old Saw Mill River Road, Tarrytown, New York.

5. On information and belief, Defendant Amgen Inc. ("Amgen") is a corporation organized and existing under the laws of the State of Delaware with its principal place of business located at One Amgen Center Drive, Thousand Oaks, California.

6. On information and belief, Defendant Immunex Corporation ("Immunex") is a wholly-owned subsidiary of Amgen.

Jurisdiction and Venue

7. This is an action for a declaratory judgment arising under 28 U.S.C. § 2201, *et seq*.

8. The Court has subject matter jurisdiction with respect to Sanofi and Regeneron's claim pursuant to 28 U.S.C. §§ 1331 and 1338.

9. Pursuant to 28 U.S.C. §§ 1391 and 1400, venue properly lies in this Court because a substantial part of the events giving rise to the parties' dispute occurred within this judicial district and Amgen and Immunex have an established place of business in this judicial district.

10. This Court has personal jurisdiction over Amgen and Immunex because their contacts with Massachusetts are continuous and systematic. On information and belief, Amgen and Immunex maintain large research and development facilities in Massachusetts; own property in Massachusetts; maintain numerous employees in Massachusetts; solicit and conduct business in Massachusetts; are registered to do business in Massachusetts; have appointed agents for the

service of process in Massachusetts; and have regularly used the Massachusetts courts for litigation, including patent enforcement actions.

Relevant Facts

Dupixent®: A Breakthrough Treatment for a Debilitating Disease

11. Sanofi and Regeneron are pharmaceutical companies dedicated to the discovery, development, and commercialization of novel medicines.

12. Dupixent®, the product at issue in this action, is a monoclonal antibody that was developed using Regeneron's revolutionary VelocImmune® mouse technology. Regeneron and Sanofi invested many years of research efforts and hundreds of millions of dollars in developing Dupixent®.

13. After receiving a "Breakthrough Therapy" designation from the U.S. Food and Drug Administration ("FDA") in 2014, Dupixent® underwent extensive clinical trials in patients suffering from uncontrolled, moderate-to-severe forms of atopic dermatitis.

14. A type of eczema, atopic dermatitis is a debilitating, disfiguring disease characterized by chronically inflamed lesions that cover the affected person's skin. These lesions result in severe itching of the skin and predispose the affected person to recurrent skin infections. Atopic dermatitis is an incurable life-long disease that, in many cases, also causes anxiety, depression, and suicidal ideation.

15. Dupixent® is a game-changer in the fight against atopic dermatitis. This is underscored by the stunning results Dupixent® achieved in clinical trials. Within two weeks of beginning treatment, most patients reported relief of their symptoms. And, by the end of the treatment cycle, nearly 40 percent of participants saw all or almost all of their skin lesions disappear. As the *New York Times* reported, because "[t]here has never been a safe and effective

treatment" for atopic dermatitis, Dupixent® now "offer[s] hope to the estimated 1.6 million adult Americans" that are affected by the condition.

16. On July 29, 2016, Regeneron submitted a Biologics License Application (BLA) for Dupixent® to the FDA and received a so-called "PDUFA date"[1] of March 29, 2017. Sanofi and Regeneron plan to make the product available to patients as soon as possible after receiving an approval from the FDA.

Amgen's Failed AMG-317 Project and the '487 Patent

17. On information and belief, in the 2000s, Amgen attempted to develop a monoclonal antibody treatment for asthma. Amgen produced a monoclonal antibody that reportedly inhibited the activity of interleukin 4 (IL-4) and interleukin 13 (IL-13), two cytokines involved in the immune response. Amgen's antibody—known under the code name AMG-317—underwent clinical trials for the treatment of moderate to severe asthma.

18. The clinical efficacy of AMG-317 failed to meet the FDA's criteria for "phase 2" trials, with patients receiving treatment with AMG-317 reporting only small improvements relative to placebo. Specifically, AMG-317 "did not demonstrate clinical efficacy across the overall group of patients." *See* Corren, *et al.*, "A Randomized, Controlled, Phase 2 Study of AMG 317, an IL-4α Antagonist, in Patients with Asthma," *Am. J. Respir. Crit. Care Med.* (181):788-96 (2010).

19. Based on these disappointing results, Amgen thereafter abandoned its development of AMG-317.

20. Amgen's failed drug-development efforts, however, did result in a number of patents, including the '487 Patent, which is titled "Anti-interleukin-4 receptor antibodies." Issued

[1] Prescription Drug User Fee Act (PDUFA) dates are deadlines by which the FDA must review new drug applications.

on March 25, 2014, the '487 Patent is assigned to Immunex and names Richard J. Armitage, Jose Carlos Escobar, and Arvia E. Morris as inventors. On information and belief, when Amgen completed its acquisition of Immunex on July 16, 2002, Amgen concomitantly acquired the rights to Immunex's portfolio of patents and patent applications, which now includes the '487 Patent.

The Present Controversy

21. Amgen has a long history of aggressively enforcing its patents against competitors like Sanofi and Regeneron, and, indeed, the parties are currently engaged in an unrelated patent litigation concerning Sanofi and Regeneron's product Praluent®.

22. Just days ago, counsel for Regeneron and Sanofi learned that Amgen has hired litigation counsel to prosecute a patent infringement litigation related to Amgen's work on antibodies to the IL-4 receptor and is in the process of retaining experts.

23. Given that Dupixent® is the only IL-4 inhibitor expected to come to market in the near future, Regeneron and Sanofi believe that Amgen and Immunex will sue them for infringement of the claims of the '487 Patent at a time of defendants' choosing and for the purpose of impairing plaintiffs' ability to sell Dupixent® in the United States. This course of conduct would be consistent with the manner in which Amgen commenced litigation with respect to Praluent®.

24. Because, as explained below, Dupixent® does not in fact infringe the '487 Patent, Sanofi and Regeneron wish to eliminate any potential obstacle Amgen might seek to raise against the planned U.S. commercialization of Dupixent®.

25. An actual, imminent, concrete, and particularized dispute exists between parties having adverse legal interests with respect to the '487 Patent. This controversy warrants relief under 28 U.S.C. §§ 2201 and 2202.

Dupixent® Does Not Infringe the '487 Patent

26. Dupixent® falls outside the claims of the '487 Patent.

27. Among other things, all 17 claims of the '487 Patent recite, expressly or by incorporation, the limitation "[a]n isolated human antibody that competes with a reference antibody for binding to [the IL-4 receptor]."

28. As it is used in the '487 Patent and as it would be understood by a person of ordinary skill in the art, the term "antibody" is a generic term that does not denote any particular structure, much less a structure that is sufficiently definite. This is underscored by certain of the dependent claims, which purport to claim the "antibody of claim 1" wherein such antibody is a "*fragment* of an antibody" or even "a fusion protein."

29. Furthermore, the activity of the "antibody" recited in the claims of the '487 Patent is described in purely functional terms. That is, the claims describe the claimed "antibody" purely based on a desired result, *i.e.*, "compet[ition]" for binding to the IL-4 receptor.

30. Because, as recited in all of the claims of the '487 Patent, the term "antibody" fails to provide sufficient structure for the functional limitation "that competes with a reference antibody for binding to human IL-4 interleukin-4 (IL-4) receptor," the term "antibody" must be construed in accordance with 35 U.S.C. § 112 ¶ 6.

31. Properly construed, none of the claims of the '487 Patent cover matter beyond the structures specifically disclosed in the specification, *i.e.*, the sequences of mAbs 6-2, 12B5, 27A1, 5A1, 63, or 1B7, the only structures conceivably capable of performing the "compet[ing]" function, or their equivalents.

32. Because Dupixent® is markedly different structurally from mAbs 6-2, 12B5, 27A1, 5A1, 63, or 1B7, and any embodiments that may qualify as equivalent, Dupixent® does not infringe any of the 17 claims of the '487 Patent.

Count I—Declaration of Non-Infringement

33. Sanofi and Regeneron repeat and reallege the allegations of paragraphs 1 through 32, as though fully set forth herein.

34. Regeneron has manufactured and will continue to manufacture Dupixent® in the United States.

35. Sanofi and Regeneron have a reasonable apprehension that Amgen and Immunex will sue them for infringement of the claims of the '487 Patent at a time of defendants' choosing and for the purpose of impairing plaintiffs' ability to sell Dupixent® in the United States. Sanofi and Regeneron's apprehension of suit is based on, among other things, (1) Amgen's prior conduct, including the parties' previous litigation history with respect to Praluent®; (2) Amgen's long history of aggressively enforcing its patents and; and (3) the fact that Amgen has hired litigation counsel to prosecute a patent infringement litigation related to Amgen's work on antibodies to the IL-4 receptor.

36. An actual, imminent, concrete, and particularized dispute exists between parties having adverse legal interests with respect to the '487 Patent. This controversy warrants relief under 28 U.S.C. §§ 2201 and 2202.

37. Accordingly, Sanofi and Regeneron are entitled to a declaratory judgment that they have not infringed, will not infringe, and are not liable for infringement of any claim of the '487 Patent, and that the commercial manufacture, use, offer for sale, sale or importation of Dupixent® would not infringe any claim of the '487 Patent, either literally or under the doctrine of equivalents.

WHEREFORE, Sanofi and Regeneron respectfully request that this Court grant relief against Amgen and Immunex in the form of a judgment:

A. Declaring that Plaintiffs have not infringed, will not infringe, and are not liable for infringement of any valid and enforceable claim of the ’487 Patent, and that the commercial manufacture, use, offer for sale, sale or importation of Dupixent® would not infringe any valid and enforceable claim of the ’487 Patent, either literally or under the doctrine of equivalents;

B. Declaring this case exceptional under 35 U.S.C. § 285 and awarding Sanofi and Regeneron’s attorneys’ fees, costs, and disbursements as a result of this action; and

C. Awarding Sanofi and Regeneron such further relief as the Court deems just and proper.

Dated: March 20, 2017

Respectfully submitted,

/s/ David L. Evans

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