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AMGEN MANUFACTURING, LIMITED

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

AMGEN INC. and AMGEN MANUFACTURING, LIMITED Plaintiffs, vs. TANVEX BIOPHARMA USA, INC., TANVEX BIOPHARMA, INC., and TANVEX BIOLOGICS CORP., Defendants.	Case No. '19CV1374 AJB MSB **COMPLAINT FOR PATENT INFRINGEMENT** **JURY TRIAL DEMANDED**

Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Plaintiffs"), by and through their undersigned attorneys, for their Complaint against Defendants Tanvex BioPharma USA, Inc. ("Tanvex"), Tanvex BioPharma, Inc., and Tanvex Biologics Corp. (collectively, "Defendants") hereby allege as follows:

NATURE OF THE ACTION

1. This is an action for patent infringement arising under the patent laws of the United States, Title 35, United States Code, including 35 U.S.C. § 271(e)(2)(C), which was enacted in 2010 as part of the Biologics Price Competition and Innovation Act of 2009 ("the BPCIA"), Pub. L. No. 111-148, §§ 7001-7003, 124 Stat. 119, 804-21 (2010) (amending, inter alia, 35 U.S.C. § 271 and 42 U.S.C. § 262).

2. The asserted patent is United States Patent No. 9,856,287 ("the '287 Patent"), attached hereto as Exhibit 1. Amgen is the owner of all rights, title, and interest in the '287 Patent. The '287 Patent claims methods of refolding recombinant proteins used in the manufacture of a biological product.

3. The BPCIA created an abbreviated pathway for the approval of biosimilar versions of approved biologic drugs. 42 U.S.C. § 262(k). The abbreviated pathway (also known as "the subsection (k) pathway") allows a biosimilar applicant (here, Tanvex BioPharma USA, Inc., acting in concert with Tanvex BioPharma, Inc. and Tanvex Biologics Corp.) to rely on the prior licensure and approval status of the innovative biological product (here, NEUPOGEN®) that the biosimilar purports to copy. Amgen is the sponsor of the reference product ("reference product sponsor" or "RPS"), NEUPOGEN®, which is approved by the U.S. Food and Drug Administration ("FDA") to decrease the incidence of infection in patients receiving myelosuppressive anti-cancer drugs. Under the subsection (k) pathway, the biosimilar applicant may rely on its reference product's data rather than demonstrating that the proposed biosimilar product is safe, pure, and potent, as Amgen was required to do to obtain FDA licensure of its reference product under 42 U.S.C. § 262(a).

4. To avoid burdening the courts and parties with unnecessary disputes, the BPCIA also creates an intricate and carefully orchestrated set of procedures for the biosimilar applicant and the RPS to engage in a series of information exchanges

and good-faith negotiations between parties prior to the filing of a patent infringement lawsuit. These exchanges are set forth in 42 U.S.C. § 262(*l*)(2)-(*l*)(5) and culminate in an "immediate patent infringement action" pursuant to 42 U.S.C. § 262(*l*)(6).

5. Seeking the benefits of the subsection (k) pathway, Tanvex BioPharma USA, Inc. acting in concert with Tanvex BioPharma, Inc. and Tanvex Biologics Corp., submitted Defendants' abbreviated Biologics License Application No. 761126 (the "Tanvex aBLA") to FDA pursuant to the BPCIA, specifically 42 U.S.C. § 262(k), requesting that its biological product ("the Tanvex Filgrastim Product") be licensed by relying on Amgen's demonstration that NEUPOGEN® (filgrastim) is "safe, pure, and potent."

6. Upon information and belief, Tanvex BioPharma USA, Inc., acting in concert with each of the other Defendants, submitted the Tanvex aBLA to FDA on or about September 30, 2018, and thus before the expiration of the '287 Patent.

7. Upon information and belief, FDA notified Tanvex that the Tanvex aBLA had been accepted for review on or about November 27, 2018.

8. In December 2018, Amgen and Tanvex began exchanging information as required by the BPCIA as detailed *infra* in ¶¶ 61-73.

9. The '287 Patent was included on Amgen's February 15, 2019 disclosure pursuant to 42 U.S.C. § 262(*l*)(3)(A).

10. Under 35 U.S.C. § 271(e)(2)(C), the submission of "an application seeking approval of a biological product" for the purpose of obtaining FDA approval to engage in commercial manufacture, use, or sale, including any amendments or supplementations thereto constitutes one or more acts of infringement: (i) with respect to a patent that is identified in the list of patents described in section 351(l)(3) of the Public Health Service Act (including as provided under section 351(l)(7) of such Act), or (ii) with respect to a patent that could be identified pursuant to 351(l)(3)(A)(i) of such Act if the applicant for the

application fails to provide the application and information required under section 351(l)(2)(A) of such Act. *See Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1672 (2017).

11. The submission of the Tanvex aBLA, including on information and belief, any amendments or supplementations thereto, constitutes one or more acts of infringement of one or more claims of the '287 Patent under 35 U.S.C. § 271(e)(2)(C).

12. If FDA approves the Tanvex aBLA and Defendants make, offer to sell, sell, or use the Tanvex Filgrastim Product within the United States, Defendants will also infringe one or more claims of the '287 Patent under 35 U.S.C. §§ 271(a), (b), (c), and/or (g).

THE PARTIES

13. Amgen Inc. is a corporation existing under the laws of the State of Delaware, with its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320. Amgen discovers, develops, manufactures, and sells innovative therapeutic products based on advances in molecular biology, recombinant DNA technology, and chemistry. Founded in 1980, Amgen Inc. is a pioneer in the development of biological human therapeutics. Today, Amgen Inc. is the largest biotechnology company in the world, fueled in part by the success of NEUPOGEN® (filgrastim).

14. Amgen Manufacturing, Limited ("AML") is a corporation existing under the laws of the Territory of Bermuda with its principal place of business at Road 31 km 24.6, Juncos, Puerto Rico 00777. AML manufactures and sells biologic medicines for treating particular diseases in humans. AML is a wholly-owned subsidiary of Amgen Inc.

15. Upon information and belief, Tanvex BioPharma USA, Inc. is a corporation organized and existing under the laws of the State of California, with its principal places of business in San Diego, California at 10394 Pacific Center Court,

San Diego, CA 92121 and in Irvine, California at 2030 Main Street #1050, Irvine, CA 92614. Upon information and belief, acting in concert with each of the other Defendants, Tanvex BioPharma USA, Inc. is in the business of developing, manufacturing, and marketing biopharmaceutical products that are intended to be distributed and sold in the State of California and throughout the United States.

16. Upon information and belief, Tanvex BioPharma, Inc. is a corporation organized and existing under the laws of the Cayman Islands, with its principal place of business in Taipei City 106, Taiwan at 13F.-1, No. 376, Sec. 4, Ren'ai Rd., D'an Dist., Taipei City 106, Taiwan. Upon information and belief, acting in concert with each of the other Defendants, Tanvex BioPharma, Inc. is in the business of developing, manufacturing, and marketing biopharmaceutical products that are intended to be distributed and sold in the State of California and throughout the United States.

17. Upon information and belief, Tanvex Biologics Corp. is a corporation organized and existing under the laws of Taiwan with its principal place of business in New Taipei City 221, Taiwan at 33F, No. 99, Sec. 1, Xintai 5th Road, Xizhi District, New Taipei City 221, Taiwan. Upon information and belief, acting in concert with each of the other Defendants, Tanvex Biologics Corp. is in the business of developing biopharmaceutical products that are intended to be distributed and sold in the State of California and throughout the United States.

18. Upon information and belief, Tanvex BioPharma USA, Inc. and Tanvex Biologics Corp. are wholly-owned subsidiaries of Tanvex BioPharma, Inc. See Exhibit 2, page 71:
http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20(EN).pdf ("Tanvex has two wholly-owned and invested subsidiaries, 'Tanvex BioPharma USA, Inc.' located in U.S. and 'Tanvex Biologics Corporation' located in Taiwan.").

19. Upon information and belief, Defendants collaborate to develop,

manufacture, seek regulatory approval for, import, market, distribute, and sell biopharmaceutical products (including products intended to be sold as biosimilar versions of successful biopharmaceutical products developed by others) in the State of California and throughout the United States.

JURISDICTION AND VENUE

20. This action arises under the patent laws of the United States, Title 35 of the United States Code, Title 42 of the United States Code, and under the Declaratory Judgment Act of 1934 (28 U.S.C. §§ 2201-2202), Title 28 of the United States Code.

21. This Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

22. Venue is proper in this Court pursuant to 28 U.S.C. § 1391(b) and (c), and 28 U.S.C. § 1400(b).

23. This Court has personal jurisdiction over each of the Defendants for the reasons set forth below.

A. Tanvex BioPharma USA, Inc.

24. Upon information and belief, Tanvex BioPharma USA, Inc., Tanvex BioPharma, Inc., and Tanvex Biologics Corp. hold themselves out as a unitary entity and represent to the public that their activities are directed, controlled, and carried out as a single entity. *See, e.g.*, Exhibit 3, Press Release, Tanvex BioPharma, Inc. "FDA Accepts TX01 BLA Filing" (Nov. 28, 2018) ("About Tanvex . . . Tanvex BioPharma, Inc. is registered in Cayman Islands and has operations and facilities in Irvine, CA, San Diego, CA, and Taipei, Taiwan").

25. Upon information and belief, Tanvex BioPharma USA, Inc. develops, manufactures, seeks regulatory approval to market, distribute, and sell biopharmaceuticals for sale and use throughout the United States, including in California and this federal judicial District.

26. Upon information and belief, Tanvex BioPharma USA, Inc. is a

corporation organized and existing under the laws of the State of California.

27. Upon information and belief, Tanvex BioPharma USA, Inc. maintains offices and manufacturing facilities at 10421 Pacific Center Court, Suite 100 and San Diego, CA 92121 and 10394 Pacific Center Court, San Diego, CA 92121.

28. Moreover, upon information and belief, Tanvex BioPharma USA, Inc., following any FDA approval of the Tanvex Filgrastim Product, will sell the Tanvex Filgrastim Product that is produced by a method that is the subject of the patent infringement claims in this action in California and throughout the United States.

29. In addition, upon information and belief, Tanvex BioPharma USA, Inc. operates as a subsidiary of Tanvex BioPharma, Inc., which exercises considerable control over Tanvex BioPharma USA, Inc. *See* Exhibit 2, (calling Tanvex BioPharma USA, Inc. its "U.S. Subsidiary"), http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20(EN).pdf.

B. Tanvex BioPharma, Inc.

30. Upon information and belief, Tanvex BioPharma, Inc., Tanvex BioPharma USA, Inc., and Tanvex Biologics Corp. hold themselves out as a unitary entity and represent to the public that their activities are directed, controlled, and carried out as a single entity. *See, e.g.*, Ex. 3, Press Release, Tanvex BioPharma, Inc. "FDA Accepts TX01 BLA Filing" (Nov. 28, 2018) ("About Tanvex . . . Tanvex BioPharma, Inc. is registered in Cayman Islands and has operations and facilities in Irvine, CA, San Diego, CA, and Taipei, Taiwan").

31. Upon information and belief, Tanvex BioPharma, Inc. collaborates with Tanvex BioPharma USA, Inc. and Tanvex Biologics Corp. to develop, manufacture, and seek approval to sell FDA-approved biopharmaceutical drugs, which are to be marketed, distributed, and sold in California and throughout the United States.

32. Upon information and belief, Tanvex BioPharma, Inc. exercises considerable control over each of the other Defendants with respect to biosimilar

products, and approves significant decisions of each of the other Defendants such as allowing Tanvex BioPharma USA, Inc. to act as the agent for Tanvex BioPharma, Inc. in connection with preparing and filing the Tanvex aBLA, and acting as Tanvex BioPharma, Inc.'s agent in the United States. For example, the Tanvex BioPharma USA, Inc. Management Team includes Allen Chao. Upon information and belief, Allen Chao is the CEO and Director of the Board of Tanvex BioPharma, Inc., and CEO and Chairman of Tanvex BioPharma USA, Inc.

33. Upon information and belief, Tanvex BioPharma, Inc. is actively involved with planning Tanvex BioPharma USA, Inc.'s new products and filing the Tanvex aBLA for the proposed biosimilar product in dispute. For example, Tanvex BioPharma, Inc. released a press release about the submission of the Tanvex aBLA to the FDA and its investor reports discuss the Tanvex aBLA extensively.

34. Upon information and belief, Tanvex BioPharma, Inc. acted in concert with each of the other Defendants to develop a proposed biosimilar version of Plaintiffs' NEUPOGEN® (filgrastim). Upon information and belief, Tanvex BioPharma, Inc. acted in concert with, directed, and/or authorized Tanvex BioPharma USA, Inc. to file the Tanvex aBLA and to seek approval from FDA to market and sell the Tanvex Filgrastim Product in the State of California and throughout the United States, which directly gives rise to Plaintiffs' claims of patent infringement. For example, Tanvex BioPharma, Inc. issued a press release on October 1, 2018 stating that "Tanvex BioPharma, Inc. (TWSE: 6541) announced the submission of its biologics license application (BLA) to the U.S. Food and Drug Administration (FDA) for TX-01, a proposed biosimilar to the reference product Neupogen® (filgrastim)." *See* "Tanvex BioPharma Submits its First Biologics License Application to U.S. FDA for TX-01" (Oct. 1, 2018), http://www.tanvex.com/PDF/News/100118.pdf, attached hereto as Exhibit 4.

35. Tanvex BioPharma, Inc. has issued press releases regarding the Tanvex Filgrastim Product and its regulatory status: *See* Press Release, Tanvex BioPharma,

Inc. "Tanvex BioPharma Submits its First Biologics License Application to U.S. FDA For TX-01" (Oct. 1, 2018), http://www.tanvex.com/PDF/News/100118.pdf, attached hereto as Exhibit 4; Press Release, Tanvex BioPharma, Inc. "Tanvex biopharma announced today (08/24/2017) the successful completion of the phase III clinical trial for TX01, a proposed biosimilar of US-licensed Neupogen (filgrastim)" (Aug. 24, 2017), http://www.tanvex.com/PDF/News/082417.pdf, attached hereto as Exhibit 5; Press Release, Tanvex, BioPharma, Inc., "Tanvex BioPharma, Inc. Announces Initiation of Pivotal Trial of TX01 (a Proposed Biosimilar of Neupogen®)," (Oct. 3, 2016), http://www.tanvex.com/PDF/News/082417.pdf, attached hereto as Exhibit 6.

36. According to a press release on Tanvex BioPharma, Inc.'s website, attached hereto as Exhibit 6, "Tanvex BioPharma, Inc. is engaged in the development, production/manufacturing, and marketing of biosimilar products. An international company registered in Cayman Islands with operations and facilities in Irvine, CA, San Diego, CA, and Taipei, Taiwan, Tanvex has end-to-end in-house development and manufacturing capabilities."

37. Additionally, and in the alternative, Plaintiffs allege that to the extent Tanvex BioPharma, Inc. is not subject to the jurisdiction of the courts of general jurisdiction of the State of California, Tanvex BioPharma, Inc. likewise is not subject to the jurisdiction of the courts of general jurisdiction of any state, and accordingly is amenable to service of process based on its aggregate contacts with the United States, including but not limited to the above described contacts, as authorized by Rule 4(k)(2) of the Federal Rules of Civil Procedure.

C. Tanvex Biologics Corp.

38. Upon information and belief, Tanvex Biologics Corp., Tanvex BioPharma USA, Inc., and Tanvex BioPharma, Inc. hold themselves out as a unitary entity and represent to the public that their activities are directed, controlled, and carried out as a single entity. *See, e.g.*, Ex. 3, Press Release, Tanvex

BioPharma, Inc. "FDA Accepts TX01 BLA Filing" (Nov. 28, 2018) ("About Tanvex . . . Tanvex BioPharma, Inc. is registered in Cayman Islands and has operations and facilities in Irvine, CA, San Diego, CA, and Taipei, Taiwan").

39. Upon information and belief, Tanvex Biologics Corp. collaborates with Tanvex BioPharma USA, Inc. and Tanvex BioPharma, Inc. to develop biopharmaceutical drugs, which are to be marketed, distributed, and sold in California and throughout the United States.

40. In addition, upon information and belief, Tanvex Biologics Corp. operates as a subsidiary of Tanvex BioPharma, Inc., which exercises considerable control over Tanvex Biologics Corp. *See* Ex. 2 at 1, (calling Tanvex Biologics Corp. its "Taiwan Subsidiary"), http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20(EN).pdf.

41. Upon information and belief, Tanvex Biologics Corp. is actively involved with planning Tanvex BioPharma USA, Inc.'s new products. For example, Tanvex BioPharma, Inc.'s 2018 Annual Report stated that the "Main Duties" of Tanvex Biologics Corp. include "New drug development" and "Initial stage process development," including "upstream and downstream initial stage process development and scale-up for mammalian cell products, including upstream cell cultivation and downstream protein purification process development." *See* Ex. 3, at 14, http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20(EN).pdf.

42. Tanvex BioPharma, Inc.'s 2016 Annual Report lists as a "Material Contract[]" the "Service agreement" between Tanvex BioPharma USA, Inc. (formerly known as La Jolla Biologics) and Tanvex Biologics Corp., under which Tanvex BioPharma USA, Inc. "provides R&D services to Tanvex Taiwan" (*i.e.*, Tanvex Biologics Corp.). *See* Exhibit 7 at 69. Tanvex BioPharma, Inc's 2018 Annual Report lists as a "Material Contract[]" the "Master Collaboration Agreement and SOW" between Tanvex BioPharma USA, Inc. and Tanvex

Biologics Corp. for "Collaboration on the biosimilar products development" and which spans from January 1, 2018 to December 31, 2022. *See* Exhibit 2, at 61-62.

43. Upon information and belief, Tanvex Biologics Corp. acted in concert with Tanvex BioPharma USA, Inc. and Tanvex BioPharma, Inc. to develop a proposed biosimilar version of Plaintiffs' NEUPOGEN® (filgrastim). Upon information and belief, Tanvex Biologics Corp. acted in concert with each of the other Defendants to file the Tanvex aBLA and to seek approval from FDA to market and sell the Tanvex Filgrastim Product in the state of California and throughout the United States, which directly gives rise to Plaintiffs' claims of patent infringement.

44. Additionally, and in the alternative, Plaintiffs allege that to the extent Tanvex Biologics Corp. is not subject to the jurisdiction of the courts of general jurisdiction of the State of California, Tanvex Biologics Corp. likewise is not subject to the jurisdiction of the courts of general jurisdiction of any state, and accordingly is amenable to service of process based on its aggregate contacts with the United States, including but not limited to the above described contacts, as authorized by Rule 4(k)(2) of the Federal Rules of Civil Procedure.

BACKGROUND

A. Amgen's Innovative Biological Product: NEUPOGEN® (filgrastim)

45. Amgen is one of the world's leading biopharmaceutical companies and is dedicated to using discoveries in human biology to invent, develop, manufacture, and sell new therapeutic products for the benefit of patients suffering from serious illnesses. Toward that end, Amgen has invested billions of dollars into its research and development efforts.

46. In 1991, Amgen first received FDA approval for NEUPOGEN® (filgrastim), pursuant to Biologics Licensing Application ("BLA") No. 103353, for decreasing the incidence of infection, as manifested by febrile neutropenia, in patients with nonmyeloid malignancies receiving myelosuppressive anticancer

drugs associated with a significant incidence of severe neutropenia with fever. FDA later approved several additional indications for the therapeutic use of NEUPOGEN® (filgrastim), including the treatment of patients with severe chronic neutropenia, patients with acute myeloid leukemia receiving induction or consolidation chemotherapy, patients receiving bone marrow transplant, and patients undergoing peripheral blood progenitor cell collection and therapy.

47. The active ingredient in NEUPOGEN® is filgrastim, a recombinantly expressed, 175-amino acid form of a protein known as human granulocyte-colony stimulating factor or "G-CSF." NEUPOGEN® (filgrastim) is also known as recombinant methionyl human granulocyte-colony stimulating factor.

48. NEUPOGEN® (filgrastim) is indicated to decrease the incidence of infection in patients receiving myelosuppressive anti-cancer drugs. By binding to specific receptors on the surface of certain types of cells, NEUPOGEN® (filgrastim) stimulates the production of a type of white blood cells known as neutrophils. Neutrophils are the most abundant type of white blood cells and form a vital part of the human immune system. A deficiency in neutrophils is known as neutropenia, a condition which makes the individual highly susceptible to infection. Neutropenia can result from a number of causes; it is a common side effect of chemotherapeutic drugs used to treat certain forms of cancer. NEUPOGEN® (filgrastim) counteracts neutropenia.

49. The availability of NEUPOGEN® (filgrastim) represented a major advance in cancer treatment by protecting chemotherapy patients from the harmful effects of neutropenia and by thus facilitating more effective chemotherapy regimens.

50. Prior to 2010, any other company wishing to sell its own version of NEUPOGEN® (filgrastim) would have had to undertake the same extensive effort to conduct clinical trials to prove to FDA that its proposed version was also safe, pure, and potent.

51. Developing a new therapeutic product from scratch is extremely expensive: studies estimate the cost of obtaining FDA approval of a new biologic product at more than $2.5 billion. *See* DiMasi J.A. *et al*., Innovation in the pharmaceutical industry: New estimates of R&D costs, 47 J. Health Econ. 20, 25-26 (2016), attached hereto as Exhibit 8.

52. Amgen Inc. is the sponsor of the BLA for NEUPOGEN® (filgrastim).

53. AML is a wholly-owned subsidiary of Amgen Inc. AML manufactures NEUPOGEN® (filgrastim).

54. Amgen USA Inc. is a wholly-owned subsidiary of Amgen Inc. Amgen USA Inc. purchases NEUPOGEN® (filgrastim) from AML, and is the distributor of NEUPOGEN® (filgrastim) in the United States.

55. Plaintiffs profit from each sale of NEUPOGEN® (filgrastim) in the United States.

B. Tanvex Seeks Approval to Market a Proposed Biosimilar Version of NEUPOGEN® (filgrastim) by Taking Advantage of the Abbreviated Subsection (k) Pathway of the BPCIA

56. Upon information and belief, Tanvex, acting in concert with each of the other Defendants, submitted the Tanvex aBLA with FDA pursuant to Section 351(k) of the Public Health Service Act in order to obtain approval to commercially manufacture, use, offer to sell, sell, and import into the United States the Tanvex Filgrastim Product, a proposed biosimilar version of Plaintiffs' NEUPOGEN® (filgrastim) product.

57. Upon information and belief, Defendants sought FDA approval for their Filgrastim Product by submitting the Tanvex aBLA under the abbreviated licensing pathway of 42 U.S.C. § 262(k), which allows Defendants to reference and rely on the approval and licensure of Plaintiffs' NEUPOGEN® (filgrastim) product in support of their request for FDA approval.

58. Upon information and belief, the Tanvex Filgrastim Product is designed to copy and compete with Plaintiffs' NEUPOGEN® (filgrastim).

59. Upon information and belief, Defendants did not seek to independently demonstrate to FDA that their biological product is "safe, pure, and potent" pursuant to 42 U.S.C. § 262(a), as Amgen did in its BLA for its innovative biological product NEUPOGEN® (filgrastim). Rather, upon information and belief, Defendants submitted an aBLA requesting that FDA evaluate the suitability of their proposed biosimilar product for licensure, expressly electing and seeking reliance on Amgen's FDA license for NEUPOGEN® (filgrastim). Accordingly, Tanvex's application is based upon publicly available information regarding FDA's previous licensure determination that NEUPOGEN® (filgrastim) is "safe, pure, and potent." 42 U.S.C. § 262(k)(2)(A)(iii)(I).

60. The Tanvex aBLA is predicated on Plaintiffs' trailblazing efforts. Defendants have publicly announced that they submitted the Tanvex aBLA under the subsection (k) pathway to obtain approval to commercially manufacture, use, offer to sell, sell, and/or import into the United States the Tanvex Filgrastim Product that they assert is a biosimilar version of Plaintiffs' NEUPOGEN®. *See* Exhibit 4, Tanvex Press Release.

C. The Information Exchange Under 42 U.S.C. § 262(*l*)

61. On December 10, 2018, Tanvex, through its counsel, sent a letter to Amgen providing notice that the Tanvex aBLA "had been accepted for review by FDA" on November 27, 2018 and "offer[ing] confidential access to copies of the materials identified in 42 U.S.C. § 262(*l*)(2)(A)-(B) relating to [the Tanvex Filgrastim Product]."

62. Under 42 U.S.C. § 262(*l*)(2)(A), Tanvex was required to provide to Amgen "a copy of the application submitted to [the FDA] under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application." Tanvex provided a copy of the Tanvex aBLA to Amgen on December 17, 2018, pursuant to § 262(*l*)(2)(A), but Tanvex did not provide batch records referenced in the Tanvex

aBLA or other manufacturing information pursuant to § 262(*l*)(2)(A).

63. On January 17, 2019, counsel for Amgen requested that Tanvex produce by February 1, 2019 the missing batch records and other manufacturing information. On February 1, 2019, Tanvex produced two batch records that were not included in the December 17, 2018 production but no other manufacturing information pursuant to § 262(*l*)(2)(A).

64. On February 15, 2019, Amgen provided Tanvex, pursuant to 42 U.S.C. § 262(*l*)(3)(A), with a list of patents for which Amgen believes a claim of patent infringement could reasonably be asserted with respect to the making, using, offering to sell, or importing into the United States of the Tanvex Filgrastim Product, pursuant to 42 U.S.C. § 262(*l*)(3)(A). This list included the '287 Patent.

65. On April 1, 2019, Tanvex, citing 42 U.S.C. § 262(*l*)(8)(A), provided "Amgen with notice that Tanvex intends to commence commercial marketing of [the Tanvex Filgrastim Product] . . . no earlier than 180 days from the date of this letter."

66. On April 12, 2019, Tanvex provided Amgen with its detailed statement pursuant to 42 U.S.C. § 262(*l*)(3)(B) (the "(3)(B) Statement"). Amgen understands that Tanvex elected not to provide Amgen with a list of patents as provided in 42 U.S.C. § 262(*l*)(3)(B)(i). Rather, Tanvex elected to fulfill its obligation under 42 U.S.C. § 262(*l*)(3)(B)(ii) pursuant to subparagraph (B)(ii)(I) by providing "a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the opinion of [Tanvex] that [the listed patents] are invalid, unenforceable, or will not be infringed by the commercial marketing of [the Tanvex Filgrastim Product]."

67. Tanvex's (3)(B) Statement relied on engineering information but not all such information was provided to Amgen in either the December 17, 2018 aBLA production or the additional production of batch records on February 1, 2019. On May 10, 2019, Amgen requested the information discussed in the Tanvex (3)(B)

Statement "including all data on protein concentration measurements."

68. On a May 22, 2019 telephone call between counsel for Amgen and Tanvex, Amgen reiterated its request for such information. Counsel for Tanvex indicated that Tanvex would produce certain information that it had relied on in its (3)(B) Statement, but that it would not search for (or endeavor to determine the existence of) additional information.

69. On May 24, 2019, Tanvex produced additional documents but not the other information as Amgen had requested. On May 28, 2019, Amgen advised Tanvex that, consistent with Amgen's position on the May 22, 2019 telephone call, "under the BPCIA, Tanvex must provide the information requested by Amgen": the engineering information relied on in Tanvex's (3)(B) Statement "including all data on protein concentration measurements."

70. Upon information and belief, Amgen has not received from Tanvex "such other information that describes the process or processes used to manufacture the biological product that is the subject of such application," as requested by Amgen under 42 U.S.C. § 262(*l*)(2)(A).

71. On June 11, 2019, Amgen provided Tanvex with its detailed statement pursuant to 42 U.S.C. § 262(*l*)(3)(C) describing "on a claim by claim basis, the factual and legal basis" of Amgen's opinion that certain claims of the '287 Patent will be infringed by the commercial marketing of the biological product that is the subject of the Tanvex aBLA, and Amgen's "response to the statement concerning validity and enforceability" as to the '287 Patent in Tanvex's April 12, 2019 statement under 42 U.S.C. § 262(*l*)(3)(B).

72. On June 24, 2018, Amgen and Tanvex engaged in a negotiation under 42 U.S.C. § 262(*l*)(4)(A), which requires the parties to engage in "good faith negotiations" in an effort to "agree on which, if any, patents . . . shall be the subject of an action for patent infringement under [42 U.S.C. § 262(*l*)(6)]." Amgen and Tanvex agreed that only the '287 Patent would be the subject of an action for patent

infringement under 42 U.S.C. § 262(*l*)(6). Amgen and Tanvex reached this agreement within 15 days of beginning their negotiations under 42 U.S.C. § 262(*l*)(4)(A).

73. Amgen filed this Complaint within the time required under 42 U.S.C. § 262(l)(6) because Amgen filed this Complaint within 30 days after Amgen and Tanvex reached agreement that only the '287 Patent would be the subject of an action for patent infringement under § 262(*l*)(6).

THE PATENT-IN-SUIT: U.S. PATENT NO. 9,856,287

74. Amgen Inc. is the owner of all rights, title, and interest in the '287 Patent.

75. AML has an exclusive license under the '287 Patent. Under the exclusive license, AML possesses exclusionary rights in the '287 Patent.

76. The '287 Patent is titled "Refolding Proteins Using a Chemically Controlled Redox State." The '287 Patent was duly and legally issued on January 2, 2018 by the United States Patent and Trademark Office ("USPTO"). The inventors of the '287 Patent are Joseph Edward Shultz, Roger Hart, and Ronald Nixon Keener III.

77. The '287 Patent is directed to improved redox chemistry-based methodologies for efficiently refolding cysteine-containing proteins expressed in non-mammalian cells with increased refolding yields.

FIRST CAUSE OF ACTION

(PATENT INFRINGEMENT OF THE '287 PATENT)

78. The allegations of paragraphs 1-77 are repeated and incorporated herein by reference.

79. Upon information and belief, by their aBLA submissions to FDA, Defendants seek FDA approval under Section 351(k) of the Public Health Service Act (42 U.S.C § 262(k)) to engage in the commercial manufacture and/or sale of the Tanvex Filgrastim Product, a proposed biosimilar version of Amgen's

NEUPOGEN®.

80. Upon information and belief, Defendants intend to manufacture, use, sell, offer for sale, and/or import the Tanvex Filgrastim Product prior to the expiration of the '287 Patent.

81. Defendants committed an act or acts of infringement with respect to the '287 Patent under 35 U.S.C. § 271(e)(2)(C) when they caused Tanvex BioPharma USA, Inc. to submit the Tanvex aBLA for the purpose of obtaining FDA approval to engage in the commercial manufacture, use, or sale of the Tanvex Filgrastim Product.

82. Defendants' participation in, contribution to, inducement of, aiding or abetting the submission of the Tanvex aBLA and any amendment(s) or supplementation(s) thereto constitutes direct, contributory, or induced infringement of one or more claims of the '287 Patent under 35 U.S.C. § 271(e)(2)(C).

83. Upon information and belief, the manufacture, use, sale, offer for sale, and/or importation of the Tanvex Filgrastim Product will infringe, literally or under the doctrine of equivalents, one or more claims of the '287 Patent.

84. Pursuant to 42 U.S.C. § 262(*l*)(3)(C), Amgen has provided Tanvex with a detailed statement describing with respect to the '287 Patent, on a claim by claim basis, the factual and legal bases of Amgen's opinion that such patent will be infringed by the commercial marketing of the biological product that is the subject of the Tanvex aBLA. Amgen's detailed statement includes, refers to, and relies on confidential information that Tanvex provided to Amgen pursuant to 42 U.S.C. § 262(*l*)(2). Amgen does not repeat its detailed statement here because under 42 U.S.C. § 262(*l*)(1), Amgen is not permitted to include confidential information provided by Tanvex "in any publicly-available complaint or other pleading." *See* 42 U.S.C. § 262(*l*)(1)(F).

85. Representative Claim 16 of the '287 Patent recites:

/ / /

A method of refolding proteins expressed in a nonmammalian expression system, the method comprising:
preparing a solution comprising:
the proteins;
at least one ingredient selected from the group consisting of a denaturant, an aggregation suppressor and a protein stabilizer;
an amount of oxidant; and
an amount of reductant,
wherein the amounts of the oxidant and the reductant are related through a thiol-pair ratio and a thiol-pair buffer strength,
wherein the thiol-pair ratio is in the range of 0.001-100,
and
wherein the thiol-pair buffer strength maintains the solubility of the solution; and
incubating the solution so that at least about 25% of the proteins are properly refolded.

86. Upon information and belief and as set forth in Amgen's detailed statement pursuant to 42 U.S.C. § 262(*l*)(3)(C) that relies on the confidential information that Tanvex was willing to provide to Amgen pursuant to 42 U.S.C. § 262(*l*)(2), the process by which Defendants manufacture and/or seek to manufacture the Tanvex Filgrastim Product satisfies each limitation of at least claims 16-18 and 26-28 of the '287 Patent, literally or under the doctrine of equivalents. Defendants practice a method of refolding proteins expressed in a nonmammalian expression system: Defendants prepare a solution comprising the proteins; at least one ingredient selected from a denaturant, an aggregation suppressor and a protein stabilizer; an amount of oxidant; and an amount of reductant; Defendants incubate the solution so that at least about 25% of the proteins are properly refolded; and the amounts of the oxidant and the reductant in Defendants' solution are related through a thiol-pair ratio and a thiol-pair buffer strength. *See, e.g.*, '287 Patent, 6:46-7:18. Further, in Defendants' process, the thiol-pair ratio is in the range of 0.001-100 and wherein the thiol-pair buffer strength maintains the solubility of the solution (*i.e.*, the concentrations of oxidants and reductants result in a thiol-pair buffer strength at which the solubility of solutes recited in the claims effectuating protein refolding is maintained). Each of these

claim elements is met literally or equivalently in Defendants' process.

87. Amgen will be irreparably harmed if Defendants are not enjoined from infringing or actively inducing or contributing to infringement of one or more claims of the '287 Patent. Amgen is entitled to injunctive relief under 35 U.S.C. § 271(e)(4)(B) preventing Defendants from any further infringement. Amgen does not have an adequate remedy at law.

88. To the extent Defendants commercialize their product prior to the expiration of the '287 Patent, Amgen will also be entitled to damages under 35 U.S.C. § 284.

89. The manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of the Tanvex Filgrastim Product before the expiration of the '287 Patent will cause injury to Amgen, entitling it to damages or other monetary relief under 35 U.S.C. § 271(e)(4)(C).

SECOND CAUSE OF ACTION

(DECLARATORY JUDGMENT OF INFRINGEMENT OF THE '287 PATENT)

90. The allegations of paragraphs 1-89 are incorporated herein by reference.

91. Upon information and belief, Defendants seek FDA approval under Section 351(k) of the Public Health Service Act (42 U.S.C § 262(k)) to manufacture and sell the Tanvex Filgrastim Product, a proposed biosimilar version of Amgen's NEUPOGEN®.

92. Upon information and belief, Defendants intend to, and will, manufacture, use, offer to sell, or sell within the United States, or import into the United States, the Tanvex Filgrastim Product immediately upon FDA licensure of the Tanvex aBLA, which FDA accepted on or about November 27, 2018.

93. If Defendants manufacture, use, offer to sell, or sell within the United States, or import into the United States, the Tanvex Filgrastim Product prior to the

expiration of the ’287 Patent, Defendants will infringe one or more claims of the ’287 Patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

94. An actual controversy has arisen and now exists between the parties concerning whether the Tanvex Filgrastim Product will infringe one or more claims of the ’287 Patent.

95. Amgen is entitled to a declaratory judgment that Defendants will infringe one or more claims of the ’287 Patent by making, using, offering to sell, or selling within the United States, or importing into the United States, the Tanvex Filgrastim Product prior to the expiration of the ’287 Patent.

96. Amgen is entitled to injunctive relief under 35 U.S.C. § 283 prohibiting Defendants from making, using, offering to sell, or selling within the United States, or importing into the United States, the Tanvex Filgrastim Product prior to the expiration of the ’287 Patent. Amgen does not have an adequate remedy at law.

97. Defendants’ manufacture, use, offer for sale, or sale within the United States or importation into the United States, of the Tanvex Filgrastim Product before the expiration of the ’287 Patent will cause injury to Amgen, entitling Amgen to damages under 35 U.S.C. § 284.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court enter judgment in their favor against Defendants and grant the following relief:

A. a judgment that Defendants have infringed directly, contributed to, or induced the infringement of one or more claims of the ’287 Patent under 35 U.S.C. § 271(e)(2)(C) by submitting to FDA the Tanvex Filgrastim aBLA and any amendment(s) or supplementation(s) thereto;

B. a preliminary and/or permanent injunction that enjoins Defendants, their officers, partners, agents, servants, employees, attorneys, affiliates, divisions, subsidiaries, other related business entities, and those persons in active concert or participation with any of them from infringing the ’287 Patent, or contributing to or

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 manufacture of which infringes the '287 Patent, in accordance with 35 U.S.C. § 271 (e)(4)(B) and 35 U.S.C. § 283;

C. a judgment declaring that the manufacture, use, offer to sell, sale, distribution, or importation of the products described in the Tanvex Filgrastim aBLA would constitute infringement of one or more claims of the '287 Patent, or inducement of or contribution to such conduct, by Defendants pursuant to 35 U.S.C. § 271(a), (b), (c), and/or (g);

D. a judgment compelling Defendants to pay to Amgen damages adequate to compensate for Defendants' infringement, in accordance with 35 U.S.C. § 271 (e)(4)(C) and 35 U.S.C. § 284;

E. a declaration that this is an exceptional case and an award to Amgen of its attorneys' fees and costs pursuant to 35 U.S.C. § 285;

F. such other and further relief as this Court may deem to be just and proper.

DEMAND FOR A JURY TRIAL

Plaintiffs hereby demand a jury trial on all issues so triable.

Respectfully submitted,

Dated: July 23, 2019

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