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AMGEN MANUFACTURING, LIMITED

13 **UNITED STATES DISTRICT COURT**

14 **SOUTHERN DISTRICT OF CALIFORNIA**

15 AMGEN INC. and AMGEN  
16 MANUFACTURING, LIMITED

17 Plaintiffs,

18 vs.

19 TANVEX BIOPHARMA USA, INC.,  
20 TANVEX BIOPHARMA, INC., and  
TANVEX BIOLOGICS CORP.,

21 Defendants.

Case No. '19CV1374 AJB MSB

**COMPLAINT FOR PATENT  
INFRINGEMENT**

**JURY TRIAL DEMANDED**

22  
23  
24  
25 Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively,  
26 "Plaintiffs"), by and through their undersigned attorneys, for their Complaint against  
27 Defendants Tanvex BioPharma USA, Inc. ("Tanvex"), Tanvex BioPharma, Inc., and  
28 Tanvex Biologics Corp. (collectively, "Defendants") hereby allege as follows:

1 **NATURE OF THE ACTION**

2 1. This is an action for patent infringement arising under the patent laws  
3 of the United States, Title 35, United States Code, including 35 U.S.C. §  
4 271(e)(2)(C), which was enacted in 2010 as part of the Biologics Price Competition  
5 and Innovation Act of 2009 (“the BPCIA”), Pub. L. No. 111-148, §§ 7001-7003,  
6 124 Stat. 119, 804-21 (2010) (amending, inter alia, 35 U.S.C. § 271 and 42 U.S.C. §  
7 262).

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

12 3. The BPCIA created an abbreviated pathway for the approval of  
13 biosimilar versions of approved biologic drugs. 42 U.S.C. § 262(k). The  
14 abbreviated pathway (also known as “the subsection (k) pathway”) allows a  
15 biosimilar applicant (here, Tanvex BioPharma USA, Inc., acting in concert with  
16 Tanvex BioPharma, Inc. and Tanvex Biologics Corp.) to rely on the prior licensure  
17 and approval status of the innovative biological product (here, NEUPOGEN®) that  
18 the biosimilar purports to copy. Amgen is the sponsor of the reference product  
19 (“reference product sponsor” or “RPS”), NEUPOGEN®, which is approved by the  
20 U.S. Food and Drug Administration (“FDA”) to decrease the incidence of infection  
21 in patients receiving myelosuppressive anti-cancer drugs. Under the subsection (k)  
22 pathway, the biosimilar applicant may rely on its reference product’s data rather  
23 than demonstrating that the proposed biosimilar product is safe, pure, and potent, as  
24 Amgen was required to do to obtain FDA licensure of its reference product under  
25 42 U.S.C. § 262(a).

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

1 and good-faith negotiations between parties prior to the filing of a patent  
2 infringement lawsuit. These exchanges are set forth in 42 U.S.C. § 262(l)(2)-(l)(5)  
3 and culminate in an “immediate patent infringement action” pursuant to 42 U.S.C.  
4 § 262(l)(6).

5 5. Seeking the benefits of the subsection (k) pathway, Tanvex BioPharma  
6 USA, Inc. acting in concert with Tanvex BioPharma, Inc. and Tanvex Biologics  
7 Corp., submitted Defendants’ abbreviated Biologics License Application No.  
8 761126 (the “Tanvex aBLA”) to FDA pursuant to the BPCIA, specifically 42  
9 U.S.C. § 262(k), requesting that its biological product (“the Tanvex Filgrastim  
10 Product”) be licensed by relying on Amgen’s demonstration that NEUPOGEN®  
11 (filgrastim) is “safe, pure, and potent.”

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

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

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

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

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

1 application fails to provide the application and information required under section  
2 351(l)(2)(A) of such Act. *See Sandoz Inc. v. Amgen Inc.*, 137 S. Ct. 1664, 1672  
3 (2017).

4 11. The submission of the Tanvex aBLA, including on information and  
5 belief, any amendments or supplementations thereto, constitutes one or more acts of  
6 infringement of one or more claims of the '287 Patent under 35 U.S.C.  
7 § 271(e)(2)(C).

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

#### 12 **THE PARTIES**

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

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

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

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

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

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

21 18. Upon information and belief, Tanvex BioPharma USA, Inc. and  
22 Tanvex Biologics Corp. are wholly-owned subsidiaries of Tanvex BioPharma, Inc.  
23 See Exhibit 2, page 71:  
24 [http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20\(EN\).pdf](http://www.tanvex.com/PDF/Financial/2018%20Annual%20Report%20(EN).pdf)  
25 (“Tanvex has two wholly-owned and invested subsidiaries, ‘Tanvex BioPharma  
26 USA, Inc.’ located in U.S. and ‘Tanvex Biologics Corporation’ located in  
27 Taiwan.”).

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

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

5 **JURISDICTION AND VENUE**

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

10 21. This Court has subject matter jurisdiction pursuant to 28 U.S.C.  
11 §§ 1331 and 1338(a).

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

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

16 **A. Tanvex BioPharma USA, Inc.**

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

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

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

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

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

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

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

14 **B. Tanvex BioPharma, Inc.**

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

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

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

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

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

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

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



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

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

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

24 **C. Tanvex Biologics Corp.**

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

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

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

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

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

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

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

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

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

18 **BACKGROUND**

19 **A. Amgen’s Innovative Biological Product: NEUPOGEN® (filgrastim)**

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

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

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

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

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

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

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

1 51. Developing a new therapeutic product from scratch is extremely  
2 expensive: studies estimate the cost of obtaining FDA approval of a new biologic  
3 product at more than \$2.5 billion. See DiMasi J.A. *et al.*, Innovation in the  
4 pharmaceutical industry: New estimates of R&D costs, 47 J. Health Econ. 20, 25-26  
5 (2016), attached hereto as Exhibit 8.

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

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

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

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

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

17 56. Upon information and belief, Tanvex, acting in concert with each of  
18 the other Defendants, submitted the Tanvex aBLA with FDA pursuant to Section  
19 351(k) of the Public Health Service Act in order to obtain approval to commercially  
20 manufacture, use, offer to sell, sell, and import into the United States the Tanvex  
21 Filgrastim Product, a proposed biosimilar version of Plaintiffs' NEUPOGEN®  
(filgrastim) product.

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

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

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

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

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

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

23           62. Under 42 U.S.C. § 262(l)(2)(A), Tanvex was required to provide to  
24 Amgen “a copy of the application submitted to [the FDA] under subsection (k), and  
25 such other information that describes the process or processes used to manufacture  
26 the biological product that is the subject of such application.” Tanvex provided a  
27 copy of the Tanvex aBLA to Amgen on December 17, 2018, pursuant to  
28 § 262(l)(2)(A), but Tanvex did not provide batch records referenced in the Tanvex

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

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

7 64. On February 15, 2019, Amgen provided Tanvex, pursuant to 42 U.S.C.  
8 § 262(l)(3)(A), with a list of patents for which Amgen believes a claim of patent  
9 infringement could reasonably be asserted with respect to the making, using,  
10 offering to sell, or importing into the United States of the Tanvex Filgrastim  
11 Product, pursuant to 42 U.S.C. § 262(l)(3)(A). This list included the '287 Patent.

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

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

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

1 Statement “including all data on protein concentration measurements.”

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

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

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

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

24 72. On June 24, 2018, Amgen and Tanvex engaged in a negotiation under  
25 42 U.S.C. § 262(l)(4)(A), which requires the parties to engage in “good faith  
26 negotiations” in an effort to “agree on which, if any, patents . . . shall be the subject  
27 of an action for patent infringement under [42 U.S.C. § 262(l)(6)].” Amgen and  
28 Tanvex agreed that only the ’287 Patent would be the subject of an action for patent



1 infringement under 42 U.S.C. § 262(l)(6). Amgen and Tanvex reached this  
2 agreement within 15 days of beginning their negotiations under 42 U.S.C.  
3 § 262(l)(4)(A).

4 73. Amgen filed this Complaint within the time required under 42 U.S.C.  
5 § 262(l)(6) because Amgen filed this Complaint within 30 days after Amgen and  
6 Tanvex reached agreement that only the '287 Patent would be the subject of an  
7 action for patent infringement under § 262(l)(6).

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

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

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

13 76. The '287 Patent is titled "Refolding Proteins Using a Chemically  
14 Controlled Redox State." The '287 Patent was duly and legally issued on January  
15 2, 2018 by the United States Patent and Trademark Office ("USPTO"). The  
16 inventors of the '287 Patent are Joseph Edward Shultz, Roger Hart, and Ronald  
17 Nixon Keener III.

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

21 **FIRST CAUSE OF ACTION**

22 **(PATENT INFRINGEMENT OF THE '287 PATENT)**

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

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

1 NEUPOGEN®.

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

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

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

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

17 84. Pursuant to 42 U.S.C. § 262(l)(3)(C), Amgen has provided Tanvex  
18 with a detailed statement describing with respect to the '287 Patent, on a claim by  
19 claim basis, the factual and legal bases of Amgen's opinion that such patent will be  
20 infringed by the commercial marketing of the biological product that is the subject  
21 of the Tanvex aBLA. Amgen's detailed statement includes, refers to, and relies on  
22 confidential information that Tanvex provided to Amgen pursuant to 42 U.S.C.  
23 § 262(l)(2). Amgen does not repeat its detailed statement here because under 42  
24 U.S.C. § 262(l)(1), Amgen is not permitted to include confidential information  
25 provided by Tanvex "in any publicly-available complaint or other pleading." See  
26 42 U.S.C. § 262(l)(1)(F).

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

28 ///

1 A method of refolding proteins expressed in a nonmammalian  
2 expression system, the method comprising:  
3 preparing a solution comprising:  
4 the proteins;  
5 at least one ingredient selected from the group consisting of  
6 a denaturant, an aggregation suppressor and a protein  
7 stabilizer;  
8 an amount of oxidant; and  
9 an amount of reductant,  
10 wherein the amounts of the oxidant and the reductant  
11 are related through a thiol-pair ratio and a thiol-  
12 pair buffer strength,  
13 wherein the thiol-pair ratio is in the range of 0.001-  
14 100,  
15 and  
16 wherein the thiol-pair buffer strength maintains the  
17 solubility of the solution; and  
18 incubating the solution so that at least about 25% of the proteins  
19 are properly refolded.

20 86. Upon information and belief and as set forth in Amgen's detailed  
21 statement pursuant to 42 U.S.C. § 262(l)(3)(C) that relies on the confidential  
22 information that Tanvex was willing to provide to Amgen pursuant to 42 U.S.C.  
23 § 262(l)(2), the process by which Defendants manufacture and/or seek to  
24 manufacture the Tanvex Filgrastim Product satisfies each limitation of at least  
25 claims 16-18 and 26-28 of the '287 Patent, literally or under the doctrine of  
26 equivalents. Defendants practice a method of refolding proteins expressed in a  
27 nonmammalian expression system: Defendants prepare a solution comprising the  
28 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

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

2 87. Amgen will be irreparably harmed if Defendants are not enjoined from  
3 infringing or actively inducing or contributing to infringement of one or more  
4 claims of the '287 Patent. Amgen is entitled to injunctive relief under 35 U.S.C.  
5 § 271(e)(4)(B) preventing Defendants from any further infringement. Amgen does  
6 not have an adequate remedy at law.

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

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

14 **SECOND CAUSE OF ACTION**  
15 **(DECLARATORY JUDGMENT OF**  
16 **INFRINGEMENT OF THE '287 PATENT)**

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

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

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

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

1 expiration of the '287 Patent, Defendants will infringe one or more claims of the  
2 '287 Patent under 35 U.S.C. § 271(a), (b), (c), and/or (g).

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

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

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

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

18 **PRAYER FOR RELIEF**

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

21 A. a judgment that Defendants have infringed directly, contributed to, or  
22 induced the infringement of one or more claims of the '287 Patent under 35 U.S.C. §  
23 271(e)(2)(C) by submitting to FDA the Tanvex Filgrastim aBLA and any  
24 amendment(s) or supplementation(s) thereto;

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

1 inducing anyone to do the same, by acts including the manufacture, use, offer to sell,  
2 sale, distribution, or importation of any current or future versions of a product that  
3 infringes, or the use or manufacture of which infringes the '287 Patent, in accordance  
4 with 35 U.S.C. § 271 (e)(4)(B) and 35 U.S.C. § 283;

5 C. a judgment declaring that the manufacture, use, offer to sell, sale,  
6 distribution, or importation of the products described in the Tanvex Filgrastim aBLA  
7 would constitute infringement of one or more claims of the '287 Patent, or  
8 inducement of or contribution to such conduct, by Defendants pursuant to 35 U.S.C.  
9 § 271(a), (b), (c), and/or (g);

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

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

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

17 **DEMAND FOR A JURY TRIAL**

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

19 Respectfully submitted,

20 Dated: July 23, 2019

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