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and Amgen Manufacturing, Limited

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

AMGEN INC. and AMGEN MANUFACTURING, LIMITED, Plaintiffs, v. ADELLO BIOLOGICS, LLC, AMNEAL PHARMACEUTICALS, LLC, and AMNEAL PHARMACEUTICALS, INC. Defendants.	C.A. No. 2:18-cv-03347-CCC-MF **JURY TRIAL DEMANDED** ***Electronically Filed***

PLAINTIFFS' SECOND AMENDED
COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Plaintiffs"), by and through their undersigned attorneys, for their Complaint against Defendants Adello Biologics, LLC, Amneal Pharmaceuticals, LLC, and Amneal Pharmaceuticals, Inc. (collectively, "Defendants"), hereby allege as follows:

THE PARTIES

1. Amgen Inc. ("Amgen") 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 is a pioneer in the development of biological human therapeutics. Today, Amgen is one of the largest biotechnology companies in the world, fueled in part by the success of its NEUPOGEN® (filgrastim) biological drug product.

2. 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.

3. Upon information and belief, Adello Biologics, LLC ("Adello") is a corporation organized and existing under the laws of Delaware and registered to do business in New Jersey. Upon information and belief, Adello has its principal place of business in New Jersey, with its headquarters and research and development laboratory located at 20 New England Avenue, Piscataway, New Jersey. Upon information and belief, acting in concert with other Defendants, Adello is in the business of developing, manufacturing, and marketing biopharmaceutical products that are distributed and sold in the state of New Jersey and throughout the United States.

4. Upon information and belief, Amneal Pharmaceuticals, LLC ("Amneal") is a corporation organized and existing under the laws of Delaware and registered to do business in New Jersey. Upon information and belief, Amneal has its principal place of business in New Jersey, with its principal executive offices located at 400 Crossing Boulevard, 3rd Floor, Bridgewater, New Jersey 08807. Upon information and belief, acting in concert with other

Defendants, Amneal is in the business of developing, manufacturing, and marketing pharmaceutical products that are distributed and sold in the state of New Jersey and throughout the United States.

5. Upon information and belief, Amneal Pharmaceuticals, Inc. ("New Amneal") is a corporation organized and existing under the laws of Delaware and has its principal place of business in New Jersey, with its principal executive offices located at 400 Crossing Boulevard, 3rd Floor, Bridgewater, New Jersey 08807. Upon information and belief, New Amneal was formed as a holding company, combining the business of Amneal and Impax Laboratories, Inc. ("Impax," now Impax Laboratories, LLC). Upon information and belief, New Amneal consolidates the financial statements of Amneal and its subsidiaries, and New Amneal's consolidated financial statements are a continuation of Amneal's financial statements. Upon information and belief, at least some, if not all, board members of Amneal are also board members of New Amneal. Upon information and belief, acting in concert with other Defendants, New Amneal is in the business of developing, manufacturing, and marketing pharmaceutical products that are distributed and sold in the state of New Jersey and throughout the United States.

6. Upon information and belief, acting in concert with other Defendants, Adello develops, manufactures, and seeks regulatory approval for importing, marketing, distributing, and selling biopharmaceutical products (including products intended to be sold as biosimilar versions of successful biopharmaceutical products developed by others) in the state of New Jersey and throughout the United States.

NATURE OF THE ACTION

7. This is an action for patent infringement arising under the patent laws of the United States, Titles 35 and 42 of the United States Code, including 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), and the Declaratory Judgment Act of 1934 (28 U.S.C. §§ 2201-2202).

8. The asserted patents are U.S. Patent Nos. 8,940,878, 8,952,138, 9,643,997, and 9,856,287 (collectively, the "Asserted Patents"). Amgen is the owner of all rights, title, and interest in the Asserted Patents. AML has an exclusive license to the Asserted Patents. The Asserted Patents claim inventions useful in the manufacture of biological pharmaceutical products.

9. 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, Adello) 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") for, among other things, decreasing 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 its biosimilar product is safe, pure, and potent, as Amgen was required to do to obtain FDA licensure of NEUPOGEN® under 42 U.S.C. § 262(a).

10. 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).

11. Under this framework, the BPCIA contemplates that the subsection (k) applicant ("applicant") will provide the RPS with its abbreviated Biologics License Application ("aBLA") and manufacturing information under 42 U.S.C. § 262(*l*)(2). Under 42 U.S.C. § 262(*l*)(3)(A), not later than 60 days after the receipt of the application and information under § 262(*l*)(2), the RPS shall provide the applicant with a list of patents for which the RPS believes a claim of patent infringement could reasonably be asserted by the RPS, or by a patent owner that has granted an exclusive license to the RPS with respect to the reference product, if a person not licensed by the RPS engaged in the making, using, offering to sell, selling, or importing into the United States of the biological product that is the subject of the subsection (k) application. Then, under 42 U.S.C. § 262(*l*)(3)(B), the applicant may provide to the RPS a list of patents that it believes a claim of patent infringement could reasonably be asserted by the RPS and a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the applicant's opinion that such patent is invalid, unenforceable, or will not be infringed by the commercial marketing of the biological product that is the subject of the subsection (k) application, 42 U.S.C. § 262(*l*)(3)(B)(ii)(I), or a statement that the applicant does not intend to begin commercial marketing until such patent expires, § 262(*l*)(3)(B)(ii)(II). Under 42 U.S.C. § 262(*l*)(3)(C), for each patent that the applicant identifies on its list under § 262(*l*)(3)(B)(ii)(I), the RPS shall provide to the applicant a detailed statement that describes, on a claim by claim basis, the factual and legal basis of the RPS's opinion that such patent will be infringed by the commercial marketing of the applicant's biological product and a response to the statement concerning validity and enforceability provided under § 262(*l*)(3)(B)(ii)(I).

12. If the parties reach agreement on which patents from these lists to litigate in an infringement action, *see* 42 U.S.C. § 262(*l*)(4)(A), the BPCIA process culminates in an "immediate

patent infringement action" pursuant to 42 U.S.C. § 262(*l*)(6). If, however, the parties fail to agree on which patents to litigate, *see* 42 U.S.C. § 262(*l*)(4)(B), the BPCIA calls for each party to simultaneously exchange lists of patents that it believes should be the subject of the litigation under 42 U.S.C. § 262(*l*)(5) and allows the RPS to bring an infringement action for each patent included on such lists under 42 U.S.C. § 262(*l*)(6)(B).

13. In addition, an applicant must provide notice of commercial marketing to the RPS not later than 180 days before the date of the first commercial marketing of its biosimilar product under 42 U.S.C. § 262(*l*)(8)(A).

14. By letter dated September 11, 2017 (the "September 11, 2017 Letter"), Adello purported to provide notice, pursuant to 42 U.S.C. § 262(*l*)(8)(A), of its intent to commercially market a proposed biosimilar to NEUPOGEN® ("the Adello Filgrastim Product") "upon receiving FDA approval and no earlier than 180 days from [September 11, 2017]." *See* 42 U.S.C. § 262(k) (section 351K of the Public Health Services Act). The September 11, 2017 Letter informed Amgen that Adello took advantage of the abbreviated subsection (k) pathway in submitting its aBLA[1] ("the Adello aBLA"). Adello thus sought the benefits of the subsection (k) pathway under the BPCIA when it submitted the Adello aBLA to the FDA requesting that the Adello Filgrastim Product be licensed by relying on Amgen's demonstration that NEUPOGEN® (filgrastim) is "safe, pure, and potent." *See* 42 U.S.C. § 262(k).

15. The September 11, 2017 Letter further stated that Adello "is not required to and does not intend to provide Amgen with [the Adello aBLA] or manufacturing information

[1] The September 11, 2017 Letter purports to provide the application number for the Adello aBLA, but the number provided, BLA No. 103353, is actually the number for Amgen's Biologics License Application NEUPOGEN® (filgrastim).

contemplated by 42 U.S.C. § 262(*l*)(2)(A)." Adello thus refused to provide its aBLA and manufacturing information to Amgen as contemplated by the BPCIA despite the fact that Adello has taken advantage of the BPCIA's abbreviated subsection (k) pathway, which allows Adello to rely on the data Amgen submitted to the FDA as part of Amgen's Biologic License Application ("BLA") for NEUPOGEN® (filgrastim). *See* Press Release, *Business Wire*, "FDA Accepts Adello's Biosimilar License Application (BLA) for a Proposed Filgrastim Biosimilar," Sept. 11, 2017, http://www.businesswire.com/news/home/20170911005971/en ("Adello Press Release"), attached hereto as Exhibit 1; Adello Biologics, Sept. 11, 2017, http://adellobio.com/news/2017/fda-accepts-adellos-biosimilar-biologics-license-application-bla-for-a-proposed-filgrastim-biosimilar (providing link from Adello's corporate website to the Adello Press Release on *Business Wire*).

16. Had Adello provided Amgen with its aBLA as contemplated by 42 U.S.C. § 262(*l*)(2)(A), the Asserted Patents could have been identified under 42 U.S.C. § 262(*l*)(3)(A).

17. Adello submitted the Adello aBLA to the FDA prior to September 11, 2017, and thus before the expiration of each of the Asserted Patents.

18. Adello received FDA acceptance of the Adello aBLA for review prior to September 11, 2017.

19. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017. Upon information and belief, Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product. Upon information and belief, Amneal is responsible for marketing, selling and pricing the Adello Filgrastim Product. Upon information and belief, on May 4, 2018, Amneal and Impax combined their businesses under a holding company, New Amneal.

20. Upon information and belief, Amneal is a subsidiary of New Amneal and acts at New Amneal's direction and control. Upon information and belief, New Amneal is Amneal's sole managing member, having the sole voting power to make all of Amneal's business decisions and control its management. Thus, upon information and belief, Amneal's marketing, selling, and pricing activities of the Adello Filgrastim Product are at the direction and under the control of New Amneal.

21. Upon information and belief, Adello, acting in concert with other Defendants, intends to commercially launch—commercially manufacture, use, sell, offer for sale, and/or import—the Adello Filgrastim Product upon receiving FDA approval, and prior to the expiration of each of the Asserted Patents.

22. The submission of the Adello aBLA, including on information and belief, any amendments thereto, is an act (or acts) of infringement of one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(e)(2)(C)(ii).

23. Unless enjoined by this Court, upon information and belief, Defendants will infringe one or more claims of each of the Asserted Patents under 35 U.S.C. §§ 271(a) and 271(g) by making, using, offering to sell or selling within the United States, or importing into the United States the Adello Filgrastim Product which Adello makes by a process covered by each of the Asserted Patents, before the expiration of each of the Asserted Patents.

24. Unless enjoined by this Court, upon information and belief, Adello will infringe one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(b) by inducing Amneal and/or New Amneal to offer to sell or sell within the United States the Adello Filgrastim Product which Adello makes by a process covered by each of the Asserted Patents, before the expiration of each of the Asserted Patents.

JURISDICTION AND VENUE

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

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

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

28. Upon information and belief, Adello has its principal place of business in New Jersey and is licensed to do business in New Jersey. Adello maintains its corporate headquarters and research and development laboratory in New Jersey. Adello thus resides in this district and has a regular and established place of business in this district.

29. This Court has personal jurisdiction over Adello. Upon information and belief, Adello is an active business entity registered with the New Jersey Department of Treasury under the business identification number 0450049858. Upon information and belief, Adello maintains a corporate agent for service of process at Princeton South Corporate Center, Suite 160, 100 Charles Ewing Boulevard, Ewing New Jersey, 08628.

30. Upon information and belief, Adello regularly conducts business in the State of New Jersey, engages in other persistent courses of conduct in the State of New Jersey, and/or derives substantial revenue from services or things used or consumed in the State of New Jersey. Upon information and belief, Adello maintains its corporate headquarters in Piscataway, New Jersey, where corporate functions are conducted and where Adello's research and development laboratory is maintained. Upon information and belief, Adello corporate officers, including its chief executive officer, are located in New Jersey.

31. Upon information and belief, Amneal has its principal place of business in New Jersey and is licensed to do business in New Jersey. Amneal maintains its corporate headquarters in New Jersey. Amneal thus resides in this district and has a regular and established place of business in this district.

32. This Court has personal jurisdiction over Amneal. Upon information and belief, Amneal is an active business entity registered with the New Jersey Department of Treasury under the business identification number 0600211542. Upon information and belief, Amneal maintains a corporate agent, Chintu Patel, for service of process at 209 McLean Blvd. Paterson, New Jersey, 07504.

33. Upon information and belief, Amneal regularly conducts business in the State of New Jersey, engages in other persistent courses of conduct in the State of New Jersey, and/or derives substantial revenue from services or things used or consumed in the State of New Jersey. Upon information and belief, Amneal maintains its corporate headquarters in Bridgewater, New Jersey, where corporate functions are conducted. Upon information and belief, Amneal corporate officers, including its chief executive officer, are located in New Jersey.

34. Upon information and belief, New Amneal has its principal place of business in New Jersey and is licensed to do business in New Jersey. New Amneal maintains its corporate headquarters in New Jersey. New Amneal thus resides in this district and has a regular and established place of business in this district and, therefore, this Court has personal jurisdiction over New Amneal.

35. Upon information and belief, New Amneal regularly conducts business in the State of New Jersey, engages in other persistent courses of conduct in the State of New Jersey, and/or derives substantial revenue from services or things used or consumed in the State of New Jersey.

Upon information and belief, New Amneal maintains its corporate headquarters in Bridgewater, New Jersey, where corporate functions are conducted. Upon information and belief, New Amneal corporate officers, including its chief executive officer, are located in New Jersey.

36. Upon information and belief, Adello, acting in concert with other Defendants, develops, manufactures, markets, distributes, sells, and seeks regulatory approval for biopharmaceuticals for sale and use throughout the United States, including in this federal Judicial District. Upon information and belief, Adello and/or its affiliates or agents, acting in concert with other Defendants, will market, sell, and/or distribute the Adello Filgrastim Product throughout the United States, including in this Judicial District, and will derive substantial revenue therefrom. Defendants' infringement of the Asserted Patents under 35 U.S.C. §§ 271(a) and 271(g) and Adello's infringement under 35 U.S.C. § 271(b) are substantial controversies "of sufficient immediacy and reality to warrant the issuance of a declaratory judgment" under 28 U.S.C. § 2201. *See Medimmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 127 (2007) (quoting *Maryland Cas. Co. v. Pac. Coal & Oil Co.*, 312 U.S. 270, 273 (1941)). Adello, acting in concert with other Defendants, intends to commercially market the Adello Filgrastim Product upon receiving FDA approval, since more than 180 days have lapsed since Adello's September 11, 2017 Letter purporting to give 180-day notice of commercial marketing. Adello notified Amgen that FDA accepted the Adello aBLA for review prior to September 11, 2017. According to Adello's website, adellobio.com/pipeline, the development status of the Adello Filgrastim Product is "Filing accepted for review by FDA."

BACKGROUND

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

37. 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.

38. 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. The 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.

39. 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. 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. 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.

40. 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 3.

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

41. Upon information and belief, Adello seeks approval to commercially manufacture, use, offer to sell, sell, and import into the United States the Adello Filgrastim Product, a proposed biosimilar version of Plaintiffs' NEUPOGEN® (filgrastim) product.

42. Upon information and belief, Adello will use a bacterial expression system to manufacture its Filgrastim Product. *See* Adello Pipeline, http://adellobio.com/pipeline (last visited March 1, 2018), attached hereto as Exhibit 4.

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

44. Amgen independently demonstrated to the FDA that its biologic product NEUPOGEN® (filgrastim) is "safe, pure, and potent" pursuant to 42 U.S.C. § 262(a). Upon information and belief, Adello submitted an aBLA requesting that the FDA evaluate the suitability of its biological product for licensure, expressly electing and seeking reliance on Amgen's FDA license for NEUPOGEN® (filgrastim). Accordingly, Adello'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).

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

46. Upon information and belief, Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017, and under this agreement, Amneal is responsible for marketing, selling and pricing the Adello Filgrastim Product. Upon information and belief, Amneal acts at New Amneal's direction since New Amneal has the sole voting power to make all of Amneal's business decisions and control its management. Thus, upon information and belief, Amneal's marketing, selling, and pricing activities with respect to the Adello Filgrastim Product are at the direction and under the control of New Amneal.

47. Adello's application is predicated on Plaintiffs' trailblazing efforts. Adello has publicly announced that it submitted the Adello aBLA under the subsection (k) pathway to obtain approval to commercially manufacture, use, offer to sell, and sell, and import into the United States the Adello Filgrastim Product that it asserts is a biosimilar version of Plaintiffs' NEUPOGEN®. *See* Exhibit 1, Adello Press Release.

THE PATENTS-IN-SUIT

48. Amgen is the owner of all rights, title, and interest in U.S. Patent No. 8,940,878 ("the '878 Patent").

49. AML holds an exclusive license to the '878 Patent.

50. The '878 Patent, titled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System," was duly and legally issued on January 27, 2015 by the United States

Patent and Trademark Office ("USPTO"). A true and correct copy of the '878 Patent is attached to this Complaint as Exhibit 5.

51. Amgen is the owner of all rights, title, and interest in U.S. Patent No. 8,952,138 ("the '138 Patent").

52. AML holds an exclusive license to the '138 Patent.

53. The '138 Patent, titled "Refolding Proteins Using a Chemically Controlled Redox State," was duly and legally issued on February 10, 2015 by the USPTO. A true and correct copy of the '138 Patent is attached to this Complaint as Exhibit 6.

54. Amgen is the owner of all rights, title, and interest in the U.S. Patent No. 9,643,997 ("the '997 Patent").

55. AML holds an exclusive license to the '997 Patent.

56. The '997 Patent, titled "Capture Purification Processes for Proteins Expressed in a Non-Mammalian System," was duly and legally issued on May 9, 2017 by the USPTO. A true and correct copy of the '997 Patent is attached to this Complaint as Exhibit 7.

57. Amgen is the owner of all rights, title, and interest in U.S. Patent No. 9,856,287 ("the '287 Patent").

58. AML holds an exclusive license to the '287 Patent.

59. The '287 Patent, titled "Refolding Proteins Using a Chemically Controlled Redox State," was duly and legally issued on January 2, 2018 by the USPTO. A true and correct copy of the '287 Patent is attached to this Complaint as Exhibit 8.

CAUSES OF ACTION

COUNT I:
JUDGMENT OF INFRINGEMENT OF THE '878 PATENT

60. Plaintiffs incorporate by reference paragraphs 1-59 as if fully set forth herein.

61. Upon information and belief, Adello seeks FDA approval under Section 351(k) of the Public Health Service Act to commercially launch—commercially manufacture, use, sell, offer for sale, and/or import—the Adello Filgrastim Product, a proposed biosimilar version of Amgen's NEUPOGEN® (filgrastim) product.

62. In its September 11, 2017 Letter, Adello notified Amgen that FDA accepted the Adello aBLA for review and that Adello intends to market its Filgrastim Product upon receiving FDA approval, and more than 180 days have lapsed since Adello purported to give 180-day notice of commercial marketing. According to Adello's website, adellobio.com/pipeline, the development status of the Adello Filgrastim Product is "Filing accepted for review by FDA."

63. Adello stated that it is not required under 42 U.S.C. § 262(*l*)(2)(A) to provide its aBLA or manufacturing information to Amgen. Consequently, at the time of Amgen's filing of its Complaint (Dkt. No. 1) in this action, Amgen was unable to provide a more detailed infringement analysis for the Adello Filgrastim Product or the process(es) of its manufacture without discovery, including the Adello aBLA and other information that describes the process or processes used to manufacture the Adello Filgrastim Product.

64. After Amgen filed its Complaint (Dkt. No. 1) on March 8, 2018, Adello thereafter provided Amgen with, upon information and belief, a copy of its aBLA as it was initially provided to FDA.

65. Based on the information that Adello provided and relying, in part, on Adello's representations in its letters of April 30, 2018 and July 24, 2018, Amgen provided its Disclosure of Asserted Claims and Infringement Contentions to Adello with respect to the '878 Patent on August 3, 2018.

66. Adello provided its Non-Infringement Contentions and Invalidity Contentions on October 5, 2018.

67. Amgen filed its First Amended Complaint (Dkt. No. 50) on October 3, 2018. Consistent with its Disclosure of Asserted Claims and Infringement Contentions, in the First Amended Complaint, Amgen asserted infringement of the four patents-in-suit, including the '878 Patent, but no longer asserted infringement against thirteen additional patents that had been included in the original Complaint.

68. Amgen provided its Response to Adello's Invalidity Contentions on November 6, 2018.

69. The '878 Patent is directed to methods for purifying protein. Representative claim 7 of the '878 Patent recites:

> 7. A method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system comprising:
> (a) expressing a protein in a non-native limited solubility form in a non-mammalian cell;
> (b) lysing a non-mammalian cell;
> (c) solubilizing the expressed protein in a solubilization solution comprising one or more of the following:
> (i) a denaturant;
> (ii) a reductant; and
> (iii) a surfactant;
> (d) forming a refold solution comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of the following:
> (i) a denaturant;
> (ii) an aggregation suppressor;
> (iii) a protein stabilizer; and
> (iv) a redox component;
> (e) directly applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix;
> (f) washing the separation matrix; and
> (g) eluting the protein from the separation matrix, wherein the separation matrix is a non-affinity resin selected from the group consisting of ion exchange, mixed mode, and a hydrophobic interaction resin.

70. Upon information and belief, the process by which Adello manufactures its Filgrastim Product literally or equivalently satisfies each limitation of at least independent claim 7 and dependent claims 8, 11-12, 15-19, and 21. Adello practices a method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system. *See* Exhibit 4, Adello Pipeline. With respect to the requirement of the "expressing" step, in Adello's process, protein is expressed in a non-native limited solubility form in a non-mammalian expression system. *Id.* With respect to the requirement of the "lysing" step, in Adello's process, a non-mammalian cell is lysed. With respect to the requirement of the "solubilizing" step, in Adello's process, protein is solubilized in a solubilization solution comprising one or more of a denaturant, reductant, and surfactant. With respect to the requirement of the "forming" step, in Adello's process, a refold solution is formed comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of a denaturant, aggregation suppressor, protein stabilizer, and redox component. With respect to the requirement of the "applying" step, Adello's refold solution is applied to a separation matrix under conditions suitable for the protein to associate with the matrix. With respect to the requirement of the "washing" step, Adello's separation matrix is washed. With respect to the requirement of the "eluting" step, in Adello's process, protein is eluted from the separation matrix.

71. Upon information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States the Adello Filgrastim Product, which is made by a process that falls within the scope of one or more claims of the '878 Patent, or has done so already, before the '878 Patent expires.

72. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017, and under this agreement, Amneal is responsible for

marketing, selling and pricing the Adello Filgrastim Product, while Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product.

73. Upon information and belief, Adello had knowledge of the '878 Patent, at least, as of the filing of the Complaint on March 8, 2018. Upon information and belief, Amneal had knowledge of the '878 Patent, at least, as of the filing of the First Amended Complaint on October 3, 2018. Upon information and belief, Adello had knowledge of the '878 Patent prior to entering into the license and commercialization agreement with Amneal because the '878 Patent issued prior to Adello's execution of the agreement with Amneal. Additionally, the '878 Patent was the subject of a prior lawsuit regarding a biosimilar product of filgrastim. *See Amgen Inc., Amgen Manufacturing, Limited v. Sandoz Inc., Sandoz International GmbH, Sandoz GmbH*, Case No. 3:14-cv-04741-RS (N.D. Cal. Oct. 24, 2014).

74. Upon information and belief, Adello knows that offering for sale or selling within the United States the Adello Filgrastim Product, which Adello makes by a process that falls within the scope of one or more claims of the '878 Patent, before the '878 Patent expires constitutes infringement of one or more claims of the '878 Patent.

75. Upon information and belief, Adello has induced or will induce Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '878 Patent expires.

76. The submission of the Adello aBLA, including on information and belief, any amendments thereto, is an act (or acts) of infringement of one or more claims of the '878 Patent under 35 U.S.C. § 271(e)(2)(C)(ii).

77. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product infringes one or more claims of the '878 Patent under 35 U.S.C. §§ 271(a) and/or 271(g).

78. Adello's inducement of Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '878 Patent expires infringes one or more claims of the '878 Patent under 35 U.S.C. § 271(b).

79. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of the Adello Filgrastim Product has or will infringe one or more claims of the '878 Patent.

80. Plaintiffs are entitled to a declaratory judgment that Defendants have infringed or will infringe one or more claims of the '878 Patent by making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product before the expiration of the '878 Patent.

81. Plaintiffs are also entitled to a declaratory judgment that Adello has infringed and/or will infringe one or more claims of the '878 Patent by actively inducing Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the expiration of the '878 Patent.

82. Plaintiffs will be irreparably harmed if Defendants are not enjoined from infringing the '878 Patent. Plaintiffs do not have an adequate remedy at law and are 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 Adello Filgrastim Product before the expiration of the '878 Patent.

83. Defendants' manufacture, use, offer to sell, or sale within the United States, or importation into the United States of the Adello Filgrastim Product before the expiration of the '878 Patent will cause injury to Plaintiffs, entitling them to damages under 35 U.S.C. § 284.

84. Plaintiffs are entitled to injunctive relief under 35 U.S.C. § 271(e)(4)(B) preventing Adello from any further infringement. Plaintiffs do not have an adequate remedy at law.

COUNT II:
JUDGMENT OF INFRINGEMENT OF THE '138 PATENT

85. Plaintiffs incorporate by reference paragraphs 1-84 as if fully set forth herein.

86. Upon information and belief, Adello seeks FDA approval under Section 351(k) of the Public Health Service Act to commercially launch—commercially manufacture, use, sell, offer for sale, and/or import—the Adello Filgrastim Product, a proposed biosimilar version of Amgen's NEUPOGEN® (filgrastim) product.

87. In its September 11, 2017 Letter, Adello notified Amgen that FDA accepted the Adello aBLA for review and that Adello intends to market its Filgrastim Product upon receiving FDA approval, and more than 180 days have lapsed since Adello purported to give 180-day notice of commercial marketing. According to Adello's website, adellobio.com/pipeline, the development status of the Adello Filgrastim Product is "Filing accepted for review by FDA."

88. Adello stated that it is not required under 42 U.S.C. § 262(*l*)(2)(A) to provide its aBLA or manufacturing information to Amgen. Consequently, at the time of Amgen's filing of its Complaint (Dkt. No. 1) in this action, Amgen was unable to provide a more detailed infringement analysis for the Adello Filgrastim Product or the process(es) of its manufacture without discovery, including the Adello aBLA and other information that describes the process or processes used to manufacture the Adello Filgrastim Product.

89. After Amgen filed its Complaint (Dkt. No. 1) on March 8, 2018, Adello thereafter provided Amgen with, upon information and belief, a copy of its aBLA as it was initially provided to FDA.

90. Based on the information that Adello provided and relying, in part, on Adello's representations in its letters of April 30, 2018 and July 24, 2018, Amgen provided its Disclosure of Asserted Claims and Infringement Contentions to Adello with respect to the '138 Patent on August 3, 2018.

91. Adello provided its Non-Infringement Contentions and Invalidity Contentions on October 5, 2018.

92. Amgen filed its First Amended Complaint (Dkt. No. 50) on October 3, 2018. Consistent with its Disclosure of Asserted Claims and Infringement Contentions, in the First Amended Complaint, Amgen asserted infringement of the four patents-in-suit, including the '138 Patent, but no longer asserted infringement against thirteen additional patents that had been included in the original Complaint.

93. Amgen provided its Response to Adello's Invalidity Contentions on November 6, 2018.

94. The '138 Patent is directed to methods for refolding protein. Claim 18[2] of the '138 Patent recites:

> 18. The method of claim 1, wherein the incubation is performed under non-aerobic conditions.

95. Upon information and belief, the process by which Adello manufactures its Filgrastim Product literally or equivalently satisfies each limitation of at least claim 18. Adello practices a method of refolding a protein expressed in a non-mammalian expression system, *i.e.*, a bacterial expression system. *See* Exhibit 4, Adello Pipeline. In Adello's process, protein is present in a volume at a concentration of 2.0 g/L or greater. With respect to the requirement of the "contacting" step, in Adello's process, the protein is contacted with a refold buffer comprising a redox component comprising a final thiol-pair ratio having a range of 0.001 to 100 and a redox buffer strength of 2 mM or greater, or an equivalent thereof, and one or more of (i) a denaturant, (ii) an aggregation suppressor, and (iii) a protein stabilizer to form a refold mixture. With respect to the requirement of the "incubating" step, in Adello's process, the refold mixture is incubated, wherein the incubation of the refold mixture is performed under non-aerobic conditions. With respect to the requirement of the "isolating" step, in Adello's process, the protein is isolated from the refold mixture.

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[2] Claim 18 depends from Claim 1, which recites:

> 1. A method of refolding a protein expressed in a non-mammalian expression system and present in a volume at a concentration of 2.0 g/L or greater comprising:
>
> (a) contacting the protein with a refold buffer comprising a redox component comprising a final thiol-pair ratio having a range of 0.001 to 100 and a redox buffer strength of 2 mM or greater and one or more of:
> (i) a denaturant;
> (ii) an aggregation suppressor; and
> (iii) a protein stabilizer; to form a refold mixture;
>
> (b) incubating the refold mixture; and
>
> (c) isolating the protein from the refold mixture.

96. Upon information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States the Adello Filgrastim Product, which is made by a process that falls within the scope of one or more claims of the '138 Patent, or has done so already, before the '138 Patent expires.

97. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017, and under this agreement, Amneal is responsible for marketing, selling and pricing the Adello Filgrastim Product, while Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product.

98. Upon information and belief, Adello had knowledge of the '138 Patent, at least, as of the filing of the Complaint on March 8, 2018. Upon information and belief, Amneal had knowledge of the '138 Patent, at least, as of the filing of the First Amended Complaint on October 3, 2018. Upon information and belief, Adello had knowledge of the '138 Patent prior to entering into the license and commercialization agreement with Amneal because the '138 Patent issued prior to Adello's execution of the agreement with Amneal. Additionally, the '138 Patent was the subject of a prior lawsuit regarding a proposed biosimilar product of filgrastim. *See Amgen Inc., Amgen Manufacturing, Limited v. Apotex Inc. and Apotex Corp.*, Case No. 0:15-cv-62081 (S.D. Fla. Oct. 2, 2015).

99. Upon information and belief, Adello knows that offering for sale or selling within the United States the Adello Filgrastim Product, which Adello makes by a process that falls within the scope of one or more claims of the '138 Patent, before the '138 Patent expires constitutes infringement of the '138 Patent.

100. Upon information and belief, Adello has induced or will induce Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '138 Patent expires.

101. The submission of the Adello aBLA, including on information and belief, any amendments thereto, is an act (or acts) of infringement of one or more claims of the '138 Patent under 35 U.S.C. § 271(e)(2)(C)(ii).

102. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product infringes one or more claims of the '138 Patent under 35 U.S.C. §§ 271(a) and/or 271(g).

103. Adello's inducement of Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '138 Patent expires infringes one or more claims of the '138 Patent under 35 U.S.C. § 271(b).

104. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of the Adello Filgrastim Product has or will infringe one or more claims of the '138 Patent.

105. Plaintiffs are entitled to a declaratory judgment that Defendants have infringed or will infringe one or more claims of the '138 Patent by making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product before the expiration of the '138 Patent.

106. Plaintiffs are also entitled to a declaratory judgment that Adello has infringed and/or will infringe one or more claims of the '138 Patent by actively inducing Amneal and/or

New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the expiration of the '138 Patent.

107. Plaintiffs will be irreparably harmed if Defendants are not enjoined from infringing the '138 Patent. Plaintiffs do not have an adequate remedy at law and are 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 Adello Filgrastim Product before the expiration of the '138 Patent.

108. Defendants' manufacture, use, offer to sell, or sale within the United States, or importation into the United States of the Adello Filgrastim Product before the expiration of the '138 Patent will cause injury to Plaintiffs, entitling them to damages under 35 U.S.C. § 284.

109. Plaintiffs are entitled to injunctive relief under 35 U.S.C. § 271(e)(4)(B) preventing Adello from any further infringement. Plaintiffs do not have an adequate remedy at law.

COUNT III:
JUDGMENT OF INFRINGEMENT OF THE '997 PATENT

110. Plaintiffs incorporate by reference paragraphs 1-109 as if fully set forth herein.

111. Upon information and belief, Adello seeks FDA approval under Section 351(k) of the Public Health Service Act to commercially launch—commercially manufacture, use, sell, offer for sale, and/or import—the Adello Filgrastim Product, a proposed biosimilar version of Amgen's NEUPOGEN® (filgrastim) product.

112. In its September 11, 2017 Letter, Adello notified Amgen that FDA accepted the Adello aBLA for review and that Adello intends to market its Filgrastim Product upon receiving FDA approval, and more than 180 days have lapsed since Adello purported to give 180-day notice of commercial marketing. According to Adello's website, adellobio.com/pipeline, the development status of the Adello Filgrastim Product is "Filing accepted for review by FDA."

113. Adello stated that it is not required under 42 U.S.C. § 262(*l*)(2)(A) to provide its aBLA or manufacturing information to Amgen. Consequently, at the time of Amgen's filing of its Complaint (Dkt. No. 1) in this action, Amgen was unable to provide a more detailed infringement analysis for the Adello Filgrastim Product or the process(es) of its manufacture without discovery, including the Adello aBLA and other information that describes the process or processes used to manufacture the Adello Filgrastim Product.

114. After Amgen filed its Complaint (Dkt. No. 1) on March 8, 2018, Adello thereafter provided Amgen with, upon information and belief, a copy of its aBLA as it was initially provided to FDA.

115. Based on the information that Adello provided and relying, in part, on Adello's representations in its letters of April 30, 2018 and July 24, 2018, Amgen provided its Disclosure of Asserted Claims and Infringement Contentions to Adello with respect to the '997 Patent on August 3, 2018.

116. Adello provided its Non-Infringement Contentions and Invalidity Contentions on October 5, 2018.

117. Amgen filed its First Amended Complaint (Dkt. No. 50) on October 3, 2018. Consistent with its Disclosure of Asserted Claims and Infringement Contentions, in the First Amended Complaint, Amgen asserted infringement of the four patents-in-suit, including the '997 Patent, but no longer asserted infringement against thirteen additional patents that had been included in the original Complaint.

118. Amgen provided its Response to Adello's Invalidity Contentions on November 6, 2018.

119. The '997 Patent is directed to methods for purifying protein. Representative claim 9 of the '997 Patent recites:

> 9. A method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system comprising:
> (a) solubilizing the expressed protein in a solubilization solution comprising one or more of the following:
> (i) a denaturant;
> (ii) a reductant; and
> (iii) a surfactant;
> (b) forming a refold solution comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of the following:
> (i) a denaturant;
> (ii) an aggregation suppressor;
> (iii) a protein stabilizer; and
> (iv) a redox component;
> (c) applying the refold solution to a separation matrix under conditions suitable for the protein to associate with the matrix;
> (d) washing the separation matrix; and
> (e) eluting the protein from the separation matrix.

120. Upon information and belief, the process by which Adello manufactures its Filgrastim Product literally or equivalently satisfies each limitation of at least dependent claims 17-18, 26-27. With respect to the requirement that the protein is expressed in a non-native limited solubility form in a non-mammalian expression system, Adello practices a method of purifying a protein expressed in a non-native limited solubility form in a non-mammalian expression system. With respect to the requirement of the "solubilizing" step, in Adello's process, protein is solubilized in a solubilization solution comprising one or more of a denaturant, reductant, and surfactant. With respect to the requirement of the "forming" step, in Adello's process, a refold solution is formed comprising the solubilization solution and a refold buffer, the refold buffer comprising one or more of a denaturant, aggregation suppressor, protein stabilizer, and redox component. With respect to the requirement of the "applying" step, Adello's refold solution is applied to a separation matrix under conditions suitable for the protein to associate with the matrix. With respect to the requirement of the "washing" step, Adello's separation matrix is

washed. With respect to the requirement of the "eluting" step, in Adello's process, protein is eluted from the separation matrix.

121. Upon information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States the Adello Filgrastim Product, which is made by a process that falls within the scope of one or more claims of the '997 Patent, or has done so already, before the '997 Patent expires.

122. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017, and under this agreement, Amneal is responsible for marketing, selling and pricing the Adello Filgrastim Product, while Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product.

123. Upon information and belief, Adello had knowledge of the '997 Patent, at least, as of the filing of the Complaint on March 8, 2018. Upon information and belief, Amneal had knowledge of the '997 Patent, at least, as of the filing of the First Amended Complaint on October 3, 2018. Upon information and belief, Adello had knowledge of the '997 Patent prior to entering into the license and commercialization agreement with Amneal because the '997 Patent issued prior to Adello's execution of the agreement with Amneal.

124. Upon information and belief, Adello knows that offering for sale or selling within the United States the Adello Filgrastim Product, which Adello makes by a process that falls within the scope of one or more claims of the '997 Patent, before the '997 Patent expires constitutes infringement of one or more claims of the '997 Patent.

125. Upon information and belief, Adello has induced or will induce Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '997 Patent expires.

126. The submission of the Adello aBLA, including on information and belief, any amendments thereto, is an act (or acts) of infringement of one or more claims of the '997 Patent under 35 U.S.C. § 271(e)(2)(C)(ii).

127. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product infringes one or more claims of the '997 Patent under 35 U.S.C. §§ 271(a) and/or 271(g).

128. Adello's inducement of Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '997 Patent expires infringes one or more claims of the '997 Patent under 35 U.S.C. § 271(b).

129. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of the Adello Filgrastim Product has or will infringe one or more claims of the '997 Patent.

130. Plaintiffs are entitled to a declaratory judgment that Defendants have infringed or will infringe one or more claims of the '997 Patent by making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim Product before the expiration of the '997 Patent.

131. Plaintiffs are also entitled to a declaratory judgment that Adello has infringed and/or will infringe one or more claims of the '997 Patent by actively inducing Amneal and/or

New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the expiration of the '997 Patent.

132. Plaintiffs will be irreparably harmed if Defendants are not enjoined from infringing the '997 Patent. Plaintiffs do not have an adequate remedy at law and are 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 Adello Filgrastim Product before the expiration of the '997 Patent.

133. Defendants' manufacture, use, offer to sell, or sale within the United States, or importation into the United States of the Adello Filgrastim Product before the expiration of the '997 Patent will cause injury to Plaintiffs, entitling them to damages under 35 U.S.C. § 284.

134. Plaintiffs are entitled to injunctive relief under 35 U.S.C. § 271(e)(4)(B) preventing Adello from any further infringement. Plaintiffs do not have an adequate remedy at law.

COUNT IV:
JUDGMENT OF INFRINGEMENT OF THE '287 PATENT

135. Plaintiffs incorporate by reference paragraphs 1-134, as if fully set forth herein.

136. Upon information and belief, Adello seeks FDA approval under Section 351(k) of the Public Health Service Act to commercially launch—commercially manufacture, use, sell, offer for sale, and/or import—the Adello Filgrastim Product, a proposed biosimilar version of Amgen's NEUPOGEN® (filgrastim) product.

137. In its September 11, 2017 Letter, Adello notified Amgen that FDA accepted the Adello aBLA for review and that Adello intends to market its Filgrastim Product upon receiving FDA approval, and more than 180 days have lapsed since Adello purported to give 180-day notice of commercial marketing. According to Adello's website, adellobio.com/pipeline, the development status of the Adello Filgrastim Product is "Filing accepted for review by FDA."

138. Adello stated that it is not required under 42 U.S.C. § 262(*l*)(2)(A) to provide its aBLA or manufacturing information to Amgen. Consequently, at the time of Amgen's filing of its Complaint (Dkt. No. 1) in this action, Amgen was unable to provide a more detailed infringement analysis for the Adello Filgrastim Product or the process(es) of its manufacture without discovery, including the Adello aBLA and other information that describes the process or processes used to manufacture the Adello Filgrastim Product.

139. After Amgen filed its Complaint (Dkt. No. 1) on March 8, 2018, Adello thereafter provided Amgen with, upon information and belief, a copy of its aBLA as it was initially provided to FDA.

140. Based on the information that Adello provided and relying, in part, on Adello's representations in its letters of April 30, 2018 and July 24, 2018, Amgen provided its Disclosure of Asserted Claims and Infringement Contentions to Adello with respect to the '287 Patent on August 3, 2018.

141. Adello provided its Non-Infringement Contentions and Invalidity Contentions on October 5, 2018.

142. Amgen filed its First Amended Complaint (Dkt. No. 50) on October 3, 2018. Consistent with its Disclosure of Asserted Claims and Infringement Contentions, in the First Amended Complaint, Amgen asserted infringement of the four patents-in-suit, including the '287 Patent, but no longer asserted infringement against thirteen additional patents that had been included in the original Complaint.

143. Amgen provided its Response to Adello's Invalidity Contentions on November 6, 2018.

144. The ’287 Patent is directed to methods of refolding proteins. Representative claim 1 of the ’287 Patent recites:

> 1. A method of refolding proteins expressed in a non-mammalian expression system, the method comprising:
> contacting the proteins with a preparation that supports the renaturation of at least one of the proteins to a biologically active form, to form a refold mixture, the preparation comprising:
> 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 preparation; and
> incubating the refold mixture so that at least about 25% of the proteins are properly refolded.

145. Upon information and belief, the process by which Adello manufactures its Filgrastim Product literally or equivalently satisfies each limitation of at least claims 1, 8-10, 14-16, 23-26, and 30. Upon information and belief, Adello practices a method of refolding proteins expressed in a non-mammalian expression system, *i.e.*, a bacterial expression system. *See* Exhibit 4, Adello Pipeline. In Adello’s process, the proteins are contacted with a preparation that supports the renaturation of at least one of the proteins to a biologically active form, to form a refold mixture. In Adello’s process, the preparation comprises 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. In Adello’s process, 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 preparation. In Adello’s process, the refold mixture is incubated so that at least about 25% of the proteins are properly refolded.

146. Upon information and belief, Defendants intend to and will make, use, offer to sell, or sell within the United States, or import into the United States the Adello Filgrastim Product, which is made by a process that falls within the scope of one or more claims of the '287 Patent, or have done so already, before the '287 Patent expires.

147. Upon information and belief, Adello entered into a license and commercialization agreement with Amneal on October 1, 2017, and under this agreement, Amneal is responsible for marketing, selling and pricing the Adello Filgrastim Product, while Adello is responsible for development, regulatory filings, obtaining FDA approval, and manufacturing the Adello Filgrastim Product.

148. Upon information and belief, Adello had knowledge of the '287 Patent, at least, as of the filing of the Complaint on March 8, 2018. Upon information and belief, Amneal had knowledge of the '287 Patent, at least, as of the filing of the First Amended Complaint on October 3, 2018.

149. Upon information and belief, Adello knows that offering for sale or selling within the United States the Adello Filgrastim Product, which Adello makes by a process that falls within the scope of one or more claims of the '287 Patent, before the '287 Patent expires constitutes infringement of one or more claims of the '287 Patent.

150. Upon information and belief, Adello has induced or will induce Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '287 Patent expires.

151. The submission of the Adello aBLA, including on information and belief, any amendments thereto, is an act (or acts) of infringement of one or more claims of the '287 Patent under 35 U.S.C. § 271(e)(2)(C)(ii).

152. Defendants' making, using, offering to sell, or selling within the United States, or importing into the United States the Adello Filgrastim product will infringe one or more claims of the '287 Patent under 35 U.S.C. §§ 271(a) and/or 271(g).

153. Adello's inducement of Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the '287 Patent expires infringes one or more claims of the '287 Patent under 35 U.S.C. § 271(b).

154. An actual controversy has arisen and now exists between the parties concerning whether the manufacture, use, offering to sell, or sale within the United States or the importation into the United States of the Adello Filgrastim Product has or will infringe one or more claims of the '287 Patent.

155. Plaintiffs are entitled to a declaratory judgment that Defendants have infringed or 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 Adello Filgrastim Product before the expiration of the '287 Patent.

156. Plaintiffs are also entitled to a declaratory judgment that Adello has infringed and/or will infringe one or more claims of the '287 Patent by actively inducing Amneal and/or New Amneal to offer for sale or sell within the United States the Adello Filgrastim Product before the expiration of the '287 Patent.

157. Plaintiffs will be irreparably harmed if Defendants are not enjoined from infringing the '287 Patent. Plaintiffs do not have an adequate remedy at law and are 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 Adello Filgrastim Product before the expiration of the '287 Patent.

158. Defendants' manufacture, use, offer to sell, or sale within the United States, or importation into the United States of the Adello Filgrastim Product before the expiration of the '287 Patent will cause injury to Plaintiffs, entitling them to damages under 35 U.S.C. § 284.

159. Plaintiffs are entitled to injunctive relief under 35 U.S.C. § 271(e)(4)(B) preventing Adello from any further infringement. Plaintiffs do not have an adequate remedy at law.

DEMAND FOR A JURY TRIAL

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

PRAYER FOR RELIEF

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

A. a judgment that Defendants have infringed or will infringe one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(a);

B. a judgment that Adello has infringed or will infringe one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(b);

C. a judgment that Defendants have infringed or will infringe one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(g);

D. a judgment that Adello has infringed one or more claims of each of the Asserted Patents under 35 U.S.C. § 271(e)(2)(C)(ii);

E. a judgment compelling Defendants to pay to Plaintiffs damages or other monetary relief adequate to compensate for Defendants' infringement of each of the Asserted Patents, in accordance with 35 U.S.C. § 284;

F. a preliminary and/or permanent injunction that enjoins Defendants, as well as all officers, employees, agents, representatives, affiliates, assignees, successors, and affiliates of Defendants, and all persons acting on behalf of or at the direction of, or in concert with Defendants,

from infringing each of the Asserted Patents, or contributing to or inducing anyone to do the same, including the manufacture, use, offer to sell, sale, distribution, or importation of any current or future versions of a product that infringes, in accordance with 35 U.S.C. § 283 and 35 U.S.C. § 271(e)(4)(B);

G. a declaration that this is an exceptional case and awarding to Plaintiffs their attorney's fees and costs pursuant to 35 U.S.C. § 285, and expenses, and

H. such other relief as this Court may deem just and proper.

Dated: February 7, 2019

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RULE 11.2 CERTIFICATION

We hereby certify that, to the best of our knowledge, the following related actions and proceedings are pending:

1. *Amgen Inc., Amgen Manufacturing, Limited v. Sandoz Inc., Sandoz International GmbH, Sandoz GmbH*, No. 2018-1551 (Fed. Cir. Feb. 12, 2018) (appeal from *Amgen Inc., Amgen Manufacturing, Limited v. Sandoz Inc., Sandoz International GmbH, Sandoz GmbH*, Case No. 3:14-cv-04741-RS (N.D. Cal. Oct. 24, 2014)).

2. *Amgen Inc., Amgen Manufacturing, Limited v. Sandoz Inc., Sandoz International GmbH, Sandoz GmbH, Lek Pharmaceuticals, d.d.*, No. 2018-1552 (Fed. Cir. Feb 12, 2018) (appeal from *Amgen Inc., Amgen Manufacturing, Limited v. Sandoz Inc., Sandoz International GmbH, Sandoz GmbH, Lek Pharmaceuticals, d.d.*, Case No. 3:16-cv-02581-RS (N.D. Cal. May 12, 2016)).

3. *Amgen Inc., Amgen Manufacturing Limited v. Mylan Inc., Mylan Pharmaceuticals Inc., Mylan GmbH, Mylan N.V.*, Case No. 2:17-cv-01235-MRH (W.D. Pa. Sep. 22, 2017).

4. *Apotex Inc., Apotex Corp. v. Amgen Inc., Amgen Manufacturing Limited*, *Inter Partes Review No.* IPR2016-01542 (P.T.A.B. Aug. 8, 2015).

5. *Adello Biologics, LLC, Apotex Inc., Apotex Corp. v. Amgen Inc., Amgen Manufacturing Limited*, Post-Grant Review No. PGR2019-00001 (P.T.A.B. Oct. 1, 2018).

6. *Amgen Inc., Amgen Manufacturing Limited v. Apotex Inc., Apotex Corp.*, Case No. 18-cv-61828-WPD (S.D. Fla. Aug. 7, 2018).

7. *Amgen Inc., Amgen Manufacturing, Limited v. Hospira, Inc., Pfizer Inc.*, Case No. No. 18-01064-CFC (D. Del. July 18, 2018).

Dated: February 7, 2019

/s/ Liza M. Walsh

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RULE 201.1 CERTIFICATION

We hereby certify that the above-captioned matter is not subject to compulsory arbitration in that the Plaintiffs seek, *inter alia*, injunctive relief.

Dated: February 7, 2019

/s/ Liza M. Walsh
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