IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF FLORIDA

Case No. 18-61828-CIV-WPD/LSS

AMGEN INC. and AMGEN MANUFACTURING LIMITED,

Plaintiff,

v.

APOTEX INC. and APOTEX CORP.,

Defendant.

DEFENDANTS APOTEX INC. AND APOTEX CORP.'S ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFFS' COMPLAINT

Defendants Apotex Inc. and Apotex Corp. (collectively, "Apotex"), by and through their attorneys from Cozen O'Connor, for their Answer and Affirmative Defenses to the Complaint [D.E. 1] filed by Plaintiffs Amgen Inc. and Amgen Manufacturing, Limited (collectively, "Amgen" or "Plaintiffs") and the First Amendment by Interlineation to Complaint[1] [D.E. 49, Exhibit B] filed by Amgen, state as follows:

GENERAL DENIAL

Pursuant to Fed. R. Civ. P. 8(b)(3), Apotex denies all allegations in Plaintiffs' Complaint [D.E. 1] and First Amendment by Interlineation to Complaint [D.E. 49, Exhibit B] except those specifically admitted below.

[1] Plaintiffs amended their Complaint by Interlineation, and specifically paragraphs 38 and 39, pursuant to this Court's Order dated February 7, 2019 [D.E. 51].

THE PARTIES

1. Upon information and belief, Apotex admits that Plaintiff Amgen Inc. is a corporation existing under the laws of the State of Delaware, with its principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320. Apotex denies all remaining allegations of Paragraph 1.

2. Upon information and belief, Apotex admits that Plaintiff Amgen Manufacturing Limited ("AML") is a corporation existing under the laws of Bermuda with its principal place of business in Juncos, Puerto Rico. Apotex denies all remaining allegations of Paragraph 2.

3. Apotex admits that Apotex Inc. is a corporation organized and existing under the laws of Canada, with its principal place of business at 150 Signet Drive, Toronto, Ontario M9L 1T9, Canada. Apotex admits that Apotex Inc. develops, manufactures, and sells pharmaceuticals, including quality generic medicines. Apotex denies all remaining allegations of Paragraph 3.

4. Apotex admits that Apotex Corp. is a corporation organized and existing under the laws of Delaware, with its principal place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326. Apotex admits that Apotex Corp. markets pharmaceuticals in the United States, including quality generic medicines. Apotex denies all remaining allegations of Paragraph 4.

5. Paragraph 5 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations of Paragraph 5.

NATURE OF THE ACTION

6. Apotex admits that Plaintiffs purport to bring this action alleging infringement of United States Patent No. 9,856,287 ("the '287 patent") pursuant to Title 35 of the United States Code, including 35 U.S.C. § 271(e)(2)(C)(i). Apotex further admits that 35 U.S.C. § 271(e)(2)(C) was enacted in 2010 as part of the Biologics Price Competition and Innovation Act ("the BPCIA"). Apotex denies all remaining allegations of Paragraph 6.

BACKGROUND

A. Amgen's Innovative NEUPOGEN® and NEULASTA® Products

7. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the allegations of Paragraph 7 and therefore denies them.

8. To the extent Paragraph 8 refers to the indications for NEUPOGEN® listed in the FDA-approved package insert, that document speaks for itself. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 8 and therefore denies them.

9. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the allegations of Paragraph 9 and therefore denies them.

10. Apotex admits that the active ingredient in NEUPOGEN® is filgrastim. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 10 and therefore denies them.

11. Upon information and belief, Apotex admits that Amgen received FDA approval for NEULASTA® in 2002. To the extent Paragraph 11 refers to the indications for NEULASTA® listed in the FDA-approved package insert, that document speaks for itself. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 11 and therefore denies them.

12. Upon information and belief, Apotex admits that the active ingredient in NEULASTA® is pegfilgrastim. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 12 and therefore denies them.

13. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the allegations of Paragraph 13 and therefore denies them.

B. The BPCIA and the Prior Actions

14. The allegations contained in Paragraph 14 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations of Paragraph 14.

15. The allegations contained in Paragraph 15 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations of Paragraph 15.

16. The allegations contained in Paragraph 16 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations of Paragraph 16.

17. The allegations contained in Paragraph 17 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an

answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations of Paragraph 17.

18. Upon information and belief, Apotex admits that Amgen is the sponsor for the NEUPOGEN® and NEULASTA® reference products. To the extent Paragraph 18 refers to the indications for NEUPOGEN® and NEULASTA® listed in their respective FDA-approved package inserts, those documents speak for themselves. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 18 and therefore denies them.

19. Paragraph 19 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that pursuant to 42 U.S.C. § 262(k), Apotex submitted abbreviated Biologics License Application ("aBLA") No. 761026 (the "Apotex Pegfilgrastim aBLA") seeking FDA approval to market a biosimilar version of Amgen's NEULASTA® (pegfilgrastim) product ("the Apotex Pegfilgrastim Product), and on or about December 15, 2014, Apotex received notification from the FDA that its Pegfilgrastim aBLA had been accepted for review. The contents of Apotex Pegfilgrastim aBLA speak for themselves. Apotex denies all remaining allegations of Paragraph 19.

20. Paragraph 20 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that its Pegfilgrastim Product is biosimilar to Amgen's NEULASTA®. Apotex denies all remaining allegations of Paragraph 20.

21. The allegations contained in Paragraph 21 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an

answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations in Paragraph 21.

22. Paragraph 22 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that pursuant to 42 U.S.C. § 262(k), Apotex submitted aBLa No. 761027 (the "Apotex Filgrastim aBLA") seeking FDA approval to market a biosimilar version of Amgen's NEUPOGEN ® (filgrastim) product ("the Apotex Filgrastim Product"), and on or about February 13, 2015, Apotex received notification from the FDA that its Filgrastim aBLA had been accepted for review. The contents of Apotex Filgrastim aBLA speak for themselves. Apotex denies all remaining allegations of Paragraph 22.

23. Paragraph 23 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that its Filgrastim Product is biosimilar to Amgen's NEUPOGEN ®. Apotex denies all remaining allegations of Paragraph 23.

24. The allegations contained in Paragraph 24 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies all remaining allegations in Paragraph 24.

25. Paragraph 25 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that pursuant to 42 U.S.C. § 262(*l*)(3)(A), in letters dated February 27, 2015 and May 1, 2015, Amgen provided Apotex with a list of patents for which Amgen purported a claim of patent infringement could reasonably be asserted against the Apotex Filgrastim Product and the Apotex Pegfilgrastim Product ("Amgen's

(*l*)(3)(A) Lists"). Apotex also admits that pursuant to 42 U.S.C. § 262(*l*)(3)(B), on or about April 17, 2015 and June 29, 2015, Apotex provided Amgen with statements regarding each patent listed by Amgen under 42 U.S.C. § 262(*l*)(3)(A) in its letters dated February 27, 2015 and May 1, 2015 ("Apotex's Detailed Statements"). Apotex further admits that on or about June 16, 2015 and August 28, 2015, Amgen provided Apotex with statements as being in accordance with 42 U.S.C. § 262(*l*)(3)(C). Apotex denies all remaining allegations of Paragraph 25.

26. Paragraph 26 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that Amgen filed two patent infringement lawsuits pursuant to 42 U.S.C. § 262(*l*)(6), relating to the Apotex Pegfilgrastim aBLA and the Apotex Filgrastim aBLA (together, "Apotex's aBLAs"), and asserting United States Patent Nos. 8,952,138 (the "'138 patent"); 6,162,427 (the "'427 patent"); and 5,824,784 (the "'784 patent") following the information exchange under 42 U.S.C. § 262(*l*) between Apotex and Amgen (together, "Amgen's Patent Infringement Actions"). Amgen's filed Complaints for Amgen's Patent Infringement Actions speak for themselves. Apotex further admits that the Court subsequently entered a Joint Stipulation of Dismissal of All Claims and Counterclaims related to the '427 patent and the '784 patent. Apotex denies all remaining allegations of Paragraph 26.

27. Paragraph 27 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that Amgen's Patent Infringement Actions were consolidated. This Court's Findings of Facts and Conclusions of Law [C.A. No. 15-61631-CIV-COHN/SELTZER (consolidated with 15-62081-CIV-COHN/SELTZER) (D.E. 267)] and Final Judgment [C.A. No. 15-61631-CIV-COHN/SELTZER (consolidated with 15-62081-CIV- COHN/SELTZER) (D.E. 268)] regarding Amgen's Patent

Infringement Actions speak for themselves. Apotex admits that Amgen Appealed the Court's Final Judgment [D.E. 268], and the Federal Circuit affirmed. Apotex admits that Plaintiffs accurately quoted a portion the Federal Circuit's opinion at *Amgen Inc. v. Apotex Inc.*, 712 F. App'x 985 (2017). Apotex further admits that the Federal Circuit mandate for that case issued on December 20, 2017. Apotex denies all remaining allegations of Paragraph 27.

B. This Action

1. U.S Patent No. 9,856,287

28. Paragraph 28 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that according to the electronic records of the United States Patent and Trademark Office ("PTO"), Amgen Inc. is the assignee of the '287 patent. Apotex further admits that the '287 patent issued to Amgen on or about January 2, 2018 following the issuance of the Federal Circuit mandate for the appeal of Amgen's Patent Infringement Actions, and that what appears to be a true and correct copy of the '287 patent is attached to Plaintiffs' Complaint as Exhibit 1. Apotex denies all remaining allegations of Paragraph 28.

29. Paragraph 29 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that according to the electronic records of the PTO, Amgen Inc. is the assignee of the '287 patent. Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the remaining allegations of Paragraph 29 and therefore denies them.

30. Paragraph 30 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex lacks knowledge or information sufficient to form a belief about the truth or falsity of the allegations of Paragraph 30 and therefore denies them.

31. Paragraph 31 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that the ’287 patent is titled “Refolding Proteins Using a Chemically Controlled Redox State,” that the ’287 patent issued on or about January 2, 2018, and that the ’287 patent lists Joseph Edward Shultz, Roger Hart, and Ronald Nixon Keener, III, as inventors. Apotex denies all remaining allegations of Paragraph 31.

32. The contents of the ’287 patent speak for themselves. Apotex denies all remaining allegations of Paragraph 32.

33. Denied.

34. Paragraph 34 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that Plaintiffs have accurately quoted a portion of Claim 16 of the ’287 patent. Apotex denies all remaining allegations of Paragraph 34.

35. Paragraph 35 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex’s Filgrastim aBLA speak for themselves. Apotex denies all remaining allegations of Paragraph 35.

36. Paragraph 36 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex’s Detailed Statements speak for themselves. Apotex denies all remaining allegations of Paragraph 36.

37. Paragraph 37 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex’s Filgrastim aBLA and Non-Confidential Apotex Responsive Brief speak for itself. Apotex denies all remaining allegations of Paragraph 37.

38. Paragraph 38[2] contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex's aBLAs, Apotex's Detailed Statements, Non-Confidential Apotex Responsive Brief, and the '287 patent speak for themselves. Apotex denies all remaining allegations of Paragraph 38.

39. Paragraph 39[3] contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex's Filgrastim aBLA speak for themselves. Apotex denies all remaining allegations of Paragraph 39.

40. Paragraph 40 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, the contents of Apotex's Filgrastim aBLA speak for themselves. Apotex denies all remaining allegations of Paragraph 40.

2. Apotex's Submissions to FDA of its Pegfilgrastim aBLA and Filgrastim aBLA

41. Paragraph 41 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that it submitted the Apotex aBLAs seeking FDA approval to market biosimilar pegfilgrastim and filgrastim products. Apotex further admits that on or about December 15, 2014, it received notification from the FDA that its Apotex Pegfilgrastim aBLA had been accepted for review, and on or about February 13, 2015, Apotex received notification from the FDA that its Apotex Filgrastim aBLA had been accepted for review. The contents of Apotex's aBLAs speak for themselves. Apotex denies all remaining allegations of Paragraph 41.

42. The allegations contained in Paragraph 42 are allegations of law or characterizations of the BPCIA that require no response from Apotex. To the extent that an

[2] Plaintiffs amended their Complaint by Interlineation, and specifically paragraphs 38 and 39, pursuant to this Court's Order dated February 7, 2019 (D.E. 51).
[3] Plaintiffs amended their Complaint by Interlineation, and specifically paragraphs 38 and 39, pursuant to this Court's Order dated February 7, 2019 (D.E. 51).

answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex admits that Plaintiffs accurately quoted portions of 35 U.S.C. § 271(e)(2)(C)(i). Apotex denies all remaining allegations of Paragraph 42.

43. Paragraph 43 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that in a letter dated January 31, 2018, Amgen supplemented its (*l*)(3)(A) Lists to include the '287 patent. Apotex further admits that on or about March 2, 2018, Apotex provided Amgen with a statement regarding the supplemental '287 patent listed by Amgen in Amgen's letter dated January 31, 2018 ("Apotex's March 2018 Detailed Statement"). Apotex denies all remaining allegations of Paragraph 43.

44. Paragraph 44 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that it is seeking FDA approval to market the Apotex Pegfilgrastim Product and the Apotex Filgrastim Product. The Apobiologix website at http://www.apobiologix.com/rd/default.asp speaks for itself. Apotex denies all remaining allegations of Paragraph 44.

45. The allegations contained in Paragraph 45 are allegations or characterizations of law that require no response from Apotex. To the extent that an answer is required, Apotex denies all characterizations of the law that are inconsistent with referenced statutes and pertinent case law. Apotex denies the remaining allegations of Paragraph 45.

46. Denied.

47. Denied.

48. Paragraph 48 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that it is seeking FDA

approval to market the Apotex Pegfilgrastim Product and the Apotex Filgrastim Product. The Apobiologix website at http://www.apobiologix.com/rd/default.asp speaks for itself. Apotex denies all remaining allegations of Paragraph 48.

JURISDICTION AND VENUE

49. Paragraph 49 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that Plaintiffs purport to bring this action pursuant to Titles 28 and 35 of the United States Code. Apotex denies all remaining allegations of Paragraph 49.

50. Paragraph 50 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a) for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 50.

51. Paragraph 51 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex admits that venue is proper in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 51.

A. Apotex Inc.

52. Apotex admits that Apotex Inc. is in the business of developing, manufacturing, and seeking regulatory approval to distribute and sell quality generic medicines throughout the United States, including in the State of Florida. Apotex Inc. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 52.

53. Paragraph 53 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Inc. does not contest personal

jurisdiction in this Court for the limited purposes of this action only. Apotex denies the remaining allegations of Paragraph 53.

54. Paragraph 54 contains legal conclusions and allegations to which no answer is required. To the extent an answer is required, Apotex admits that it is seeking approval from the FDA to market its Pegfilgrastim Product and its Filgrastim Product after FDA-approval of Apotex's aBLAs. Further, Apotex Inc. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 54.

55. Paragraph 55 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Inc. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 55.

56. Paragraph 56 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Inc. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 56.

57. Apotex admits that Apotex Inc. has previously submitted to jurisdiction of this Court in the prior actions between Amgen and Apotex regarding Apotex's aBLAs for the limited purposes of those actions only. Apotex Inc. and Apotex Corp. do not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 57.

58. Apotex admits that Apotex Inc. has previously submitted to the jurisdiction of this Court in a case that is not factually related in any respect to the present action. Apotex Inc. and Apotex Corp. do not contest personal jurisdiction or venue in this Court for the limited purposes

of this action only. Apotex denies all remaining allegations of Paragraph 58.

59. Paragraph 59 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Inc. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 59.

B. Apotex Corp.

60. Paragraph 60 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Corp. admits that it is a corporation organized and existed under the laws of Delaware, with its principal place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326. Apotex does not content personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 60.

61. Apotex admits that Apotex Corp. seeks regulatory approval for, markets, distributes, and sells quality generic medicines throughout the United States, including in the State of Florida. Apotex Corp. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 61.

62. Paragraph 62 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Corp. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 62.

63. Paragraph 63 contains legal conclusions and allegations to which no answer is required. To the extent that an answer is required, Apotex Corp. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 63.

64. Apotex admits that Apotex Corp. has previously submitted to jurisdiction of this Court in the prior actions between Amgen and Apotex regarding Apotex's aBLAs for the limited purposes of those actions only. Apotex Inc. and Apotex Corp. do not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 64.

65. Apotex admits that Apotex Corp. has previously submitted to the jurisdiction of this Court in a case that is not factually related in any respect to the present action. Apotex Inc. and Apotex Corp. do not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 65.

66. Apotex admits that it is seeking approval from FDA to market its Pegfilgrastim Product after FDA-approval of Apotex's Pegfilgrastim aBLA. Apotex Corp. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 66.

67. Apotex admits that it is seeking approval from FDA to market its Filgrastim Product after FDA-approval of Apotex's Filgrastim aBLA. Apotex Corp. does not contest personal jurisdiction in this Court for the limited purposes of this action only. Apotex denies all remaining allegations of Paragraph 67.

FIRST COUNT
(INFRINGEMENT OF THE '287 PATENT (PEGFILGRASTIM))

68. Apotex incorporates by reference its answers to the allegations of paragraphs 1-67, of the Complaint as amended by interlineation, as if fully set forth herein.

69. Apotex admits that pursuant to 42 U.S.C § 262(k), Apotex is seeking FDA approval to market Apotex's Pegfilgrastim Product, a biosimilar version of Amgen's NEULASTA®. Apotex denies all remaining allegations of Paragraph 69.

70. Admitted.

71. Denied.

72. Denied.

73. Denied.

74. Denied.

75. Denied.

SECOND COUNT
(DECLARATORY JUDGMENT OF INFRINGEMENT
OF THE '287 PATENT (PEGFILGRASTIM))

76. Apotex incorporates by reference its answers to the allegations of paragraphs 1-75, of the Complaint as amended by interlineation, as if fully set forth herein.

77. Apotex admits that pursuant to 42 U.S.C § 262(k), Apotex is seeking FDA approval to market Apotex's Pegfilgrastim Product, a biosimilar version of Amgen's NEULASTA®. Apotex denies all remaining allegations of Paragraph 77.

78. Apotex admits that it is seeking approval from the FDA to market its Pegfilgrastim Product after FDA-approval of Apotex's Pegfilgrastim aBLA. Apotex further admits that on or about December 15, 2014, it received notification from FDA that its Apotex Pegfilgrastim aBLA had been accepted for review. The Apobiologix website at http://www.apobiologix.com/rd/default.asp speaks for itself. Apotex denies all remaining allegations of Paragraph 78.

79. Denied.

80. Denied.

81. Denied.

82. Denied.

THIRD COUNT
(INFRINGEMENT OF THE '287 PATENT (FILGRASTIM))

83. Apotex incorporates by reference its answers to the allegations of paragraphs 1-82, of the Complaint as amended by interlineation, as if fully set forth herein.

84. Apotex admits that pursuant to 42 U.S.C § 262(k), Apotex is seeking FDA approval to market Apotex's Filgrastim Product, a biosimilar version of Amgen's NEUPOGEN®. Apotex denies all remaining allegations of Paragraph 84.

85. Admitted.

86. Denied.

87. Denied.

88. Denied.

89. Denied.

90. Denied.

FOURTH COUNT
(DECLARATORY JUDGMENT OF INFRINGEMENT
OF THE '287 PATENT (FILGRASTIM))

91. Apotex incorporates by reference its answers to the allegations of paragraphs 1-90, of the Complaint as amended by interlineation, as if fully set forth herein.

92. Apotex admits that pursuant to 42 U.S.C § 262(k), Apotex is seeking FDA approval to market Apotex's Filgrastim Product, a biosimilar version of Amgen's NEULASTA®. Apotex denies all remaining allegations of Paragraph 92.

93. Apotex admits that it is seeking approval from FDA to market its Filgrastim Product after FDA-approval of Apotex's Filgrastim aBLA. Apotex further admits that on or about February 13, 2015, it received notification from FDA that its Apotex Filgrastim aBLA had been accepted for review. The Apobiologix website at

http://www.apobiologix.com/rd/default.asp speaks for itself. Apotex denies all remaining allegations of Paragraph 93.

94. Denied.

95. Denied.

96. Denied.

97. Denied.

PRAYER FOR RELIEF

Apotex denies that Amgen is entitled to any of the relief requested in its Prayer for Relief.

APOTEX'S AFFIRMATIVE DEFENSES

Apotex asserts the following defenses without prejudice to the denials in this Answer, without admitting any allegations of the Complaint, as amended by interlineation, not otherwise admitted.

FIRST AFFIRMATIVE DEFENSE
(Failure to State a Claim)

Amgen's Complaint, as amended by interlineation, fails to state a claim upon which relief may be granted.

SECOND AFFIRMATIVE DEFENSE
(No Infringement under 35 U.S.C. § 271(e)(2)(C)(i))

The submissions of Apotex's aBLAs seeking approval to market Apotex's Filgrastim Product and Apotex's Pegfilgrastim Product do not infringe, directly or indirectly, any valid and/or enforceable claim of the '287 patent, either literally or under the doctrine of equivalents.

THIRD AFFIRMATIVE DEFENSE
(No Direct Infringement)

Apotex has not, does not, and will not infringe, either literally or under the doctrine of equivalents, any valid and/or enforceable claim of the ’287 patent.

FOURTH AFFIRMATIVE DEFENSE
(No Indirect Infringement)

Apotex has not, does not, and will not induce the infringement of, or contribute to the infringement of, any valid and/or enforceable claim of the ’287 patent.

FIFTH AFFIRMATIVE DEFENSE
(Invalidity)

The ’287 patent and each of the claims thereof are invalid for failure to comply with one or more conditions for patentability set forth in one or more provision of 35 U.S.C. §§ 101, 102, 103, and/or 112, or other judicially-created bases for invalidation.

SIXTH AFFIRMATIVE DEFENSE

Plaintiffs are not entitled to preliminary and/or permanent equitable relief, including but not limited to a preliminary and/or permanent injunction that enjoins Apotex, its officers, partners, agents, servants, employees, attorneys, affiliates, divisions, subsidiaries, other related business entities, and those persons in active concert or participation with any of them from any commercial manufacture, use, offer to sell or sale within the United States, or importation into the United States, of any product that purportedly infringes, or the use or manufacture of which purportedly infringes the ’287 patent.

SEVENTH AFFIRMATIVE DEFENSE

Apotex’s actions in defending this case do not give rise to an exceptional case under 35 U.S.C. § 285.

RESERVATION OF DEFENSES

Apotex hereby reserves any and all defenses that are available under the Federal Rules of Civil Procedure and the U.S. Patent Laws and any other defenses, at law or in equity, that may now exist or become available later as a result of discovery and further factual investigation during this litigation.

APOTEX INC.'S AND APOTEX CORP.'S COUNTERCLAIMS

Apotex Inc. and Apotex Corp. (collectively, "Apotex"), by way of their attorneys Cozen O'Connor, hereby allege for their Counterclaims against Amgen Inc. and Amgen Manufacturing Limited (collectively, "Counterclaim Defendants" or "Amgen") the following:

THE PARTIES

1. Apotex Inc. is a corporation organized and existing under the laws of Canada, with its principal place of business at 150 Signet Drive, Toronto, Ontario M9L 1T9, Canada.

2. Apotex Corp. is a corporation organized and existing under the laws of the State of Delaware, with its principle place of business at 2400 North Commerce Parkway, Suite 400, Weston, Florida 33326.

3. Counterclaim Defendant Amgen Inc. purports to be 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.

4. Counterclaim Defendant Amgen Manufacturing Limited ("AML") purports to be a corporation existing under the laws of Bermuda with its principal place of business in Juncos, Puerto Rico.

JURISDICTION AND VENUE

5. These Counterclaims arise under the Patent Laws of the United States, 35 U.S.C. § 1 *et seq.*; the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202; and the Biologics Price Competition and Innovation Act ("BPCIA") 42 U.S.C. § 262.

6. This Court has subject matter jurisdiction over these Counterclaims under 28 U.S.C. §§ 1131, 1338(a)-(b); under the Declaratory Judgment Act, 28 U.S.C. §§ 2201, and 2202; and under the BPCIA, 42 U.S.C. § 262.

7. This Court has personal jurisdiction over each of Counterclaim Defendants, Amgen Inc. and Amgen Manufacturing Limited, at least because they have availed themselves of the rights and privileges of this forum by filing the Complaint in this judicial district.

8. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391(b) and (c) and 1400(b).

BACKGROUND

Counterclaim Defendants and Biologics

9. Counterclaim Defendants are engaged in the development, commercialization, and marketing of pharmaceutical products, including biological products, for the treatment of various disorders.

10. Before marketing a biological product in the United States, a manufacturer must submit a Biologics License Application ("BLA") and the U.S. Food and Drug Administration ("FDA") must approve it.

11. Among other things, the BLA must contain a full description of manufacturing methods and nonclinical laboratory and clinical studies which demonstrate that the manufactured product meets required safety, purity, and potency standards.

12. FDA only approves a biologic if it determines that the product meets applicable requirements to ensure safety, purity, and potency of such products.

13. On or about February 20, 1991, FDA approved Amgen's BLA No. 103353 for filgrastim, marketed under the tradename NEUPOGEN®, and on or about January 31, 2002, FDA approved Amgen's BLA No. 125031 for pegfilgrastim, marketed under the tradename NEULASTA®.

14. Amgen's 12 year market exclusivity for its NEULASTA ® and NEUPOGEN® products have expired. *See* 42 USC § 262(k)(7)(a).

Apotex and Biosimilars

15. Apotex is engaged in the development, commercialization, and marketing of generic pharmaceutical products, including biosimilars, for the treatment of various disorders.

16. Biosimilars are biological products intended to be clinically similar to a previously FDA-approved biological reference product ("reference product"). In this sense, biosimilars are like "generics" for small molecule drugs.

17. Biosimilars are licensed by the FDA under the provisions of the BPCIA.

18. Enacted in 2010 as part of the Patient Protection and Affordable Care Act, the BPCIA creates an abbreviated licensure pathway for biological products shown to be biosimilar to the reference product. *See* BPCIA §§ 7001-7003, Pub. L. No. 111-148, 124 STAT. 119, 804-21 (2010).

19. The licensure pathway is considered "abbreviated" because the biosimilar applicant (also known as a "subsection (k) applicant") is not required to provide the full scale of preclinical and clinical test data required for approval of the reference product. Rather, the biosimilar applicant must demonstrate that the biosimilar is "highly similar to the reference product notwithstanding minor differences in clinically inactive components" and that "there are

no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." *See* 42 U.S.C. § 262(i)(2).

20. Congress enacted the BPCIA with the intent to provide a "biosimilars pathway balancing innovation and consumer interests . . . ." *See* BPCIA, § 7001(b), Pub. L. No. 111-148, 124 STAT. at 804.

21. Biosimilars, like generic drugs, are expected to provide a price advantage over the reference product. Consequently, biosimilars are also expected to be utilized in an effort to control health-care costs.

22. Similarly, the introduction of biosimilars as alternatives to reference products, like the introduction of generic drugs as alternatives to brand-name drugs, is expected to reduce the market share of reference products.

23. On or about October 16, 2014, Apotex submitted BLA No. 761026 ("Apotex's Pegfilgrastim aBLA"), seeking FDA approval to market a biosimilar pegfilgrastim product, for which NEULASTA® is the reference product ("Apotex's Pegfilgrastim Product").

24. On or about December 12, 2014, Apotex submitted BLA No. 761027 ("Apotex's Filgrastim aBLA"), seeking FDA approval to market a biosimilar filgrastim product, for which NEUPOGEN® is the reference product ("Apotex's Filgrastim Product").

U.S. Patent No. 9,856,287

25. On information and belief, Amgen is the owner of U.S. Patent No. 9,856,287 ("the '287 patent").

26. The '287 patent is entitled: "Refolding Proteins Using A Chemically Controlled Redox State" and issued on January 2, 2018.

27. Two of the sole independent claims, claims 16 and 26 of the '287 patent asserted against Apotex, recite, *inter alia*, a method of refolding a protein expressed in a non-mammalian

expression system comprising a solution that requires the "amounts of the oxidant and reductant are related through a thiol-pair ratio and thiol-pair buffer strength" and "the thiol-pair buffer strength maintains the solubility of the solution." *See* '287 patent, claims 16, 26.

28. The '287 patent does not disclose a method of refolding any specific protein, much less the protein found in Apotex's Pegfilgrastim Product and Apotex's Filgrastim Product.

COUNT I
(Declaratory Judgment of Noninfringement of the '287 Patent)

29. Apotex hereby incorporates by reference each and every allegation set forth in its Answer and Affirmative Defenses to the Complaint, as amended by interlineation, and paragraphs 1-28 of these Counterclaims, as if fully set forth herein.

30. In their Complaint, Counterclaim Defendants assert that Apotex committed a statutory act of infringement under 35 U.S.C. § 271(e)(2)(C)(i) by submitting Apotex's Pegfilgrastim aBLA and Filgrastim aBLA (together, "Apotex's aBLAs") to the FDA.

31. Apotex asserts that the manufacture, use, offer for sale, sale, or importation of Apotex's Pegfilgrastim Product and Apotex's Filgrastim Product does not and will not infringe any valid claim of the '287 patent under 35 U.S.C. §§ 271(a), (b), (c), or (g), or (e)(2)(C)(i).

32. The '287 patent includes claims that purport to cover methods of refolding proteins expressed in non-mammalian expression systems and requires, *inter alia*, that the amounts of the oxidant and the reductant are related through a thiol-pair ratio and thiol-pair buffer strength and that the thiol-pair buffer strength maintains the solubility of the solution.

33. The '287 patent does not claim the method of manufacturing Apotex's Pegfilgrastim Product.

34. The '287 patent also does not claim the method of manufacturing Apotex's Filgrastim Product.

35. The method of manufacturing Apotex's Pegfilgrastim Product and Apotex's Filgrastim Product differ from the manufacturing process recited in claims 16, 17, 19, 23-27, 29, and 30 of the '287 patent ("the Asserted Claims") at least because Apotex's manufacturing process does not include the following limitations of the Asserted Claims: (i) wherein the amounts of oxidant and reductant that are related through a thiol-pair ratio and a thiol-pair buffer strength; (ii) wherein the thiol-pair buffer strength maintains the solubility of the solution; (iii) wherein the solution has a protein concentration in the solution in a range 1-40 g/L; (iv) wherein the thiol-pair buffer strength is 2 mM or greater; (v) wherein the thiol-pair ratio is calculated according to the following equation: $[\text{the reductant}]^2/[\text{the oxidant}]$; (vi) wherein the thiol-pair buffer strength is calculated according to the following equation: 2[the oxidant] + [the reductant]; and (vii) wherein the thiol-pair ratio is calculated according to the following equation $[\text{the reductant}]^2/[\text{the oxidant}]$ and the thiol-pair buffer strength is calculated according to the following equation: 2[the oxidant] + [the reductant]. *See, e.g.*, Defendants Apotex Inc. and Apotex Corp.'s Memorandum in Support of Motion to Dismiss Pursuant to Fed. R. Civ. P. 12(b)(6) (D.E. 9); *see also* Defendants Apotex Inc. and Apotex Corp.'s Reply Memorandum in Support of Motion to Dismiss Pursuant to Fed. R. Civ. P. 12(b)(6) (D.E. 50); aBLA Nos. 761026 and 761027.

36. An actual, substantial, and continuing justiciable case or controversy exists between Counterclaim Defendants and Apotex regarding infringement of the '287 patent.

37. Apotex is entitled to a declaration that the manufacture, use, offer for sale, sale, or importation of Apotex's Pegfilgrastim Product and Apotex's Filgrastim Product that are the subject of Apotex's aBLAs has not, does not, and will not infringe any valid and/or enforceable claim of the '287 patent under 35 U.S.C. §§ 271(a), (b), (c), or (g), or (e)(2)(C).

38. Such a declaration is necessary and appropriate at this time to determine the rights and obligations of the parties.

39. This is an exceptional case with respect to these Counterclaims, and Apotex is entitled to an award of attorneys' fees under 35 U.S.C. § 285.

COUNT II
(Declaratory Judgment of Invalidity of the '287 Patent)

40. Apotex hereby incorporates by reference each and every allegation set forth in its Answer and Affirmative Defenses to the Complaint, as amended by interlineation, and paragraphs 1-39 of these Counterclaims, as if fully set forth herein.

41. In their Complaint, Counterclaim Defendants assert that Apotex committed a statutory act of infringement under 35 U.S.C. § 271(e)(2)(C)(i) by submitting Apotex's aBLAs to the FDA.

42. Apotex asserts that the claims of the '287 patent are invalid for failure to comply with one or more of the conditions for patentability set forth in Title 35 of the United States Code.

43. An actual, substantial, and continuing justiciable case or controversy exists between Counterclaim Defendants and Apotex regarding the validity of the '287 patent.

44. Apotex is entitled to a declaration that the claims of the '287 patent are invalid.

45. Such a declaration is necessary and appropriate at this time to determine the rights and obligations of the parties.

PRAYER FOR RELIEF

WHEREFORE, Apotex respectfully prays that the Court enter judgment in its favor and against Amgen/Counterclaim Defendants as follows:

A. Declaring that the claims of the ’287 patent are not and will not be infringed by Apotex;

B. Declaring that the claims of the ’287 patent are invalid;

C. Granting Apotex judgment in its favor on Amgen’s Complaint, as amended by interlineation;

D. Denying any and all requests by Counterclaim Defendants for injunctive relief;

E. Dismissing Amgen’s Complaint, as amended by interlineation, with prejudice;

F. A finding that this is an exceptional case with respect to these Counterclaims, and an award of attorneys’ fees to Apotex in this action pursuant to 35 U.S.C. § 285; and

G. Awarding Apotex any other such relief as is just and proper.

April 18, 2019

Respectfully submitted

By: */s/ Simeon D. Brier*

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on this 18th day of April, 2019, I electronically filed the foregoing document with the Clerk of the Court using CM/ECF. I also certify that the foregoing document is being served this day on all counsel of record identified on the attached service list in the manner specified, either via transmission of Notices of Electronic Filing generated by CM/ECF or in some other authorized manner for those counsel or parties who are not authorized to electronically receive Notices of Electronic Filing.

/s/ Simeon D. Brier
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