

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ARAGON PHARMACEUTICALS, INC.,)	
JANSSEN BIOTECH, INC., THE)	
REGENTS OF THE UNIVERSITY OF)	
CALIFORNIA, and SLOAN-KETTERING)	
INSTITUTE FOR CANCER RESEARCH,)	
)	
Plaintiffs,)	C.A. No. _____
)	
v.)	
)	
HETERO LABS LIMITED UNIT V and)	
HETERO USA, INC.,)	
)	
Defendants.)	

COMPLAINT

Plaintiffs Aragon Pharmaceuticals, Inc. (“Aragon”), Janssen Biotech, Inc. (“JBI”), The Regents of the University of California (“Regents”), and Sloan-Kettering Institute for Cancer Research (“Sloan-Kettering”) (collectively, “Plaintiffs”), for their Complaint against Defendants Hetero Labs Limited Unit V (“Hetero Labs”) and Hetero USA, Inc. (“Hetero USA”) (collectively, “Defendants”), hereby allege as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 8,445,507 (“the 507 Patent”), 9,481,663 (“the 663 Patent”), 9,884,054 (“the 054 Patent”), 10,052,314 (“the 314 Patent”), 10,702,508 (“the 508 Patent”), and 10,849,888 (“the 888 Patent”) (collectively, the “Patents-In-Suit”).
2. This action relates to the submission of Abbreviated New Drug Application No. 217185 (“the ANDA”) by Defendants to the United States Food and Drug Administration (“FDA”)

seeking approval to market a proposed generic version of Erleada® (“Proposed ANDA Product”) prior to the expiration of the Patents-In-Suit.

THE PARTIES

3. Aragon is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 10990 Wilshire Boulevard, Suite 440, Los Angeles, California 90024.

4. JBI is a corporation organized and existing under the laws of the Commonwealth of Pennsylvania, having its principal place of business at 800/850 Ridgeview Drive, Horsham, Pennsylvania 19044.

5. Regents is a California non-profit constitutional corporation and the governing body of an educational institution, having its principal place of business at 1111 Franklin Street, Oakland, California 94607.

6. Sloan-Kettering is a corporation organized and existing under the laws of the State of New York, having its principal place of business at 1275 York Avenue, New York, New York 10065.

7. On information and belief, Hetero Labs is a corporation organized under the laws of India, having its principal place of business at Sy. No.: 439, 440, 441 & 458, TSIIC Formulation SEZ, Jadcherla Mandal, Polepally Village, Mahabubnagar, Telangana, India 509301.

8. On information and belief, Hetero USA is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 1035 Centennial Avenue, Piscataway, New Jersey 08854.

JURISDICTION AND VENUE

9. This is an action for patent infringement arising under the Patent Laws of the United States, 35 U.S.C. § 100 *et seq.*, including § 271(e)(2), and also including an action seeking declaratory judgment pursuant to the Declaratory Judgment Act, 28 U.S.C. §§ 2201-02 for patent infringement arising under 35 U.S.C. § 100 *et seq.*, including § 271(a)-(c).

10. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

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

12. On information and belief, Defendants cooperate, collaborate, or act in concert for the purposes of manufacturing, selling, marketing, distributing, and importing generic drug products in Delaware and throughout the United States.

13. On information and belief, Hetero Labs has substantial, continuous, and systematic contacts with Delaware.

14. On information and belief, Hetero Labs develops, manufactures, markets, and distributes pharmaceutical products, including generic pharmaceutical products, for sale in the State of Delaware and throughout the United States.

15. On information and belief, Hetero Labs, alone or together with Hetero USA, has committed, or aided, abetted, actively induced, contributed to, or participated in the commission of an act of patent infringement under 35 U.S.C. § 271(e)(2) that has led or will lead to foreseeable harm and injury to Plaintiffs throughout the United States, including in Delaware.

16. On information and belief, Hetero Labs consented to jurisdiction, did not contest jurisdiction, or asserted counterclaims in Delaware in one or more prior litigations, for example:

Duchesnay Inc. et al. v. Hetero Labs Limited et al., No. 21-1130; *Duchesnay Inc. et al. v. Hetero Labs Limited et al.*, No. 21-538; *Gilead Sciences, Inc. v. Apotex, Inc. et al.*, No. 20-189.

17. This Court has personal jurisdiction over Hetero Labs by virtue of, among other things, (1) its continuous and systematic contacts with Delaware; (2) its acts of patent infringement that will result in foreseeable harm in Delaware; (3) its sale of a substantial volume of prescription drugs in Delaware; and (4) its conduct by and through, and in concert with, Hetero USA.

18. This Court has personal jurisdiction over Hetero Labs because, *inter alia*, this action arises from actions of Hetero Labs directed toward Delaware. For example, Defendants submitted the ANDA seeking approval to commercially manufacture, use, sell, offer for sale, or import the Proposed ANDA Product prior to the expiration of the Patents-In-Suit. If FDA approval is obtained, the Proposed ANDA Product would be sold in Delaware, causing injury to Plaintiffs in Delaware.

19. Exercising personal jurisdiction over Hetero Labs in this district would not be unreasonable given Hetero Labs' contacts in this district and the interest in this district of resolving disputes related to products to be sold herein.

20. In the alternative, this Court has personal jurisdiction over Hetero Labs because the requirements of Federal Rule of Civil Procedure 4(k)(2)(A) are met: (a) Plaintiffs' claims arise under federal law; (b) Hetero Labs is a foreign defendant not subject to personal jurisdiction in the courts of any State; and (c) Hetero Labs has sufficient contacts with the United States as a whole, including, but not limited to, filing Abbreviated New Drug Applications with the FDA and manufacturing and selling generic pharmaceutical products that are distributed throughout the United States, such that this Court's exercise of jurisdiction over Hetero Labs satisfies due process, and is consistent with the United States Constitution and Laws.

21. Venue is proper under 28 U.S.C. § 1391(c)(3) because Hetero Labs is a foreign corporation.

22. On information and belief, Hetero USA has substantial, continuous, and systematic contacts with Delaware.

23. On information and belief, Hetero USA develops, manufactures, markets, and distributes pharmaceutical products, including generic pharmaceutical products, for sale in the State of Delaware and throughout the United States.

24. On information and belief, Hetero USA has substantial, continuous, and systematic contacts with Delaware, including that it is incorporated in Delaware (Entity File No. 4837317).

25. On information and belief, Hetero USA, alone or together with Hetero Labs, has committed, or aided, abetted, actively induced, contributed to, or participated in the commission of an act of patent infringement under 35 U.S.C. § 271(e)(2) that has led or will lead to foreseeable harm and injury to Plaintiffs throughout the United States, including in Delaware.

26. On information and belief, Hetero USA consented to jurisdiction, did not contest jurisdiction, or asserted counterclaims in Delaware in one or more prior litigations, for example: *Novartis Pharmaceuticals Corporation v. Alkem Laboratories Ltd. et al.*, No. 21-1330; *Duchesnay Inc. et al. v. Hetero Labs Limited et al.*, No. 21-1130; *Merck Sharp & Dohme Corp. v. Annora Pharma Private Limited et al.*, No. 21-1006; *Duchesnay Inc. et al. v. Hetero Labs Limited et al.*, No. 21-538; *Boehringer Ingelheim Pharmaceuticals Inc. et al. v. Annora Pharma Private Limited et al.*, No. 20-277; *Gilead Sciences, Inc. v. Apotex, Inc. et al.*, No. 20-189.

27. This Court has personal jurisdiction over Hetero USA by virtue of, among other things, (1) its incorporation in Delaware; (2) its continuous and systematic contacts with Delaware; (3) its acts of patent infringement that will result in foreseeable harm in Delaware; (4) its sale of a

substantial volume of prescription drugs in Delaware; and (5) its conduct by and through, and in concert with, Hetero Labs.

28. This Court has personal jurisdiction over Hetero USA because, *inter alia*, this action arises from actions of Hetero USA directed toward Delaware. For example, Defendants submitted the ANDA seeking approval to commercially manufacture, use, sell, offer for sale, or import the Proposed ANDA Product prior to the expiration of the Patents-In-Suit. If FDA approval is obtained, the Proposed ANDA Product would be sold in Delaware, causing injury to Plaintiffs in Delaware.

29. Exercising personal jurisdiction over Hetero USA in this district would not be unreasonable given Hetero USA's contacts in this district and the interest in this district of resolving disputes related to products to be sold herein.

30. On information and belief, Hetero USA will directly benefit if the ANDA is approved by participating in the distribution, offer for sale, or sale of the Proposed ANDA Product.

31. Venue is proper under 28 U.S.C. § 1400(b) because Hetero USA is incorporated in Delaware and thus resides in this judicial district.

ERLEADA®

32. JBI holds approved New Drug Application No. 210951 for apalutamide, which is prescribed and sold as Erleada®.

33. On information and belief, Defendants know that JBI holds approved New Drug Application No. 210951.

34. Erleada® is indicated for the treatment of patients with non-metastatic castration-resistant prostate cancer and metastatic castration-sensitive prostate cancer. Erleada® is supplied as tablets for oral administration containing the active pharmaceutical ingredient apalutamide.

35. The International Union of Pure and Applied Chemistry (IUPAC) name for apalutamide is 4-[7-(6-Cyano-5-trifluoromethylpyridin-3-yl)-8-oxo-6-thioxo-5,7-diazaspiro[3.4]oct-5-yl]-2-fluoro-N-methylbenzamide.

THE PATENTS-IN-SUIT

36. On May 21, 2013, the 507 Patent, titled “Androgen Receptor Modulator for the Treatment of Prostate Cancer and Androgen Receptor-Associated Diseases” was duly and legally issued to Regents as assignee. A copy of the 507 Patent is attached as Exhibit A.

37. On November 1, 2016, the 663 Patent, titled “Crystalline Forms of an Androgen Receptor Modulator” was duly and legally issued to Aragon and Sloan-Kettering as assignees. A copy of the 663 Patent is attached as Exhibit B.

38. On February 6, 2018, the 054 Patent, titled “Anti-androgens for the Treatment of Non-metastatic Castrate-resistant Prostate Cancer” was duly and legally issued to Aragon as assignee. A copy of the 054 Patent is attached as Exhibit C.

39. On August 21, 2018, the 314 Patent, titled “Anti-androgens for the Treatment of Non-metastatic Castrate-resistant Prostate Cancer” was duly and legally issued to Aragon as assignee. A copy of the 314 Patent is attached as Exhibit D.

40. On July 7, 2020, the 508 Patent, titled “Anti-androgens for the Treatment of Non-metastatic Castrate-resistant Prostate Cancer” was duly and legally issued to Aragon as assignee. A copy of the 508 Patent is attached as Exhibit E.

41. On December 1, 2020, the 888 Patent, titled “Anti-androgens for the Treatment of Non-metastatic Castrate-resistant Prostate Cancer” was duly and legally issued to Aragon as assignee. A copy of the 888 Patent is attached as Exhibit F.

42. Pursuant to 21 U.S.C. § 355(b)(1), the Patents-In-Suit are listed in the FDA publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (also known as the “Orange Book”) as covering Erleada®.

43. On information and belief, Defendants know that the Patents-In-Suit are listed in the Orange Book as covering Erleada®.

DEFENDANTS' NOTICE LETTER AND THE ANDA

44. By letter dated April 18, 2022, addressed to JBI, Sloan-Kettering, Aragon and Regents (“Notice Letter”), Defendants notified Plaintiffs that they had submitted ANDA No. 217185 to the FDA under § 505(j)(2) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. § 355(j)). The Notice Letter stated that the ANDA seeks the FDA approval necessary to engage in activities that constitute or require the commercial manufacture, use, sale, offer for sale in, or importation into the United States, of the Proposed ANDA Product, described in the Notice Letter as “Apalutamide Tablets; Oral 60 mg” prior to the expiration of the Patents-In-Suit.

45. The Notice Letter stated that Defendants had received a Paragraph IV acknowledgement letter from the FDA.

46. The ANDA includes a Paragraph IV Certification that the claims of the Patents-In-Suit are invalid, unenforceable, or not infringed.

47. The Notice Letter stated that the Proposed ANDA Product will not literally infringe the claims of the 663 Patent because the Proposed ANDA Product “is not the claimed polymorphic form.”

48. The Notice Letter stated that the Proposed ANDA Product will not infringe the claims of the 663 Patent under the doctrine of equivalents because the Proposed ANDA Product “is not the claimed polymorphic form.”

49. The Notice Letter included an Offer for Confidential Access (“OCA”) to the ANDA. The parties agreed on revised terms for the OCA. On May 6, 2022, Defendants produced documents that Defendants purported to be the ANDA.

50. On information and belief, the Proposed ANDA Product contains some amount of crystalline Form B of apalutamide.

51. On information and belief, the drug substance in and used for the Proposed ANDA Product contains some amount of crystalline Form B of apalutamide.

52. Plaintiffs are commencing this action within 45 days of the date of receipt of the Notice Letter.

COUNT I – CLAIM FOR INFRINGEMENT OF THE 507 PATENT

53. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.

54. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22.

55. On information and belief, because the Proposed ANDA Product contains apalutamide, the Proposed ANDA Product and the use of the Proposed ANDA Product infringe at least claims 1, 2, 3, 11, 19, and 22 of the 507 Patent.

56. On information and belief, the Proposed ANDA Product infringes at least claims 1 and 22 of the 507 Patent because it contains the compound apalutamide.

57. On information and belief, the Proposed ANDA Product infringes at least claims 2 and 11 of the 507 Patent because it is a pharmaceutical composition comprising a therapeutically effective amount of the compound apalutamide and a pharmaceutically acceptable carrier, diluent, or adjuvant.

58. On information and belief, the use of the Proposed ANDA Product will infringe at least claims 3 and 19 of the 507 Patent because physicians and/or patients will practice a method for treating a hyperproliferative disorder, specifically prostate cancer, said method comprising administering, causing to be administered, or directing the administration of the compound apalutamide to a subject, specifically a patient, in need of such treatment, thereby treating the prostate cancer.

59. On information and belief, Defendants will induce infringement of at least claims 3 and 19 of the 507 Patent by actively inducing the use of the Proposed ANDA Product to practice a method for treating a hyperproliferative disorder, specifically prostate cancer, said method comprising administering, causing to be administered, or directing the administration of the compound apalutamide to a subject, specifically a patient, in need of such treatment, thereby treating the prostate cancer.

60. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

61. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 507 Patent. The Notice Letter did not include a detailed and

supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 507 Patent.

62. On information and belief, Defendants have actual knowledge of the 507 Patent, at least as shown by the Notice Letter.

63. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, by submitting or causing to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 507 Patent.

64. On information and belief, the Proposed ANDA Product and its use, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, under at least one of 35 U.S.C. § 271(a), (b), or (c).

65. On information and belief, the manufacture, use, import, offer to sell, or sale of the Proposed ANDA Product will directly infringe the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22.

66. On information and belief, physicians and/or patients will directly infringe the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, by the use of the Proposed ANDA Product upon approval.

67. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22, for the pecuniary benefit of Defendants.

68. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22. On information and belief, Defendants will actively induce the infringement of the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22.

69. On information and belief, the Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22. On information and belief, Defendants will thus contribute to the infringement of the claims of the 507 Patent, including at least claims 1, 2, 3, 11, 19, and 22.

70. On information and belief, the actions described in this Complaint relating to the ANDA and the 507 Patent were done by and for the benefit of Defendants.

71. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

COUNT II – CLAIM FOR INFRINGEMENT OF THE 663 PATENT

72. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.

73. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 663 Patent, including at least claims 1, 13, and 17.

74. On information and belief, because the Proposed ANDA Product and the drug substance in and used for the Proposed ANDA Product contain some amount of crystalline Form B of apalutamide, the Proposed ANDA Product and the drug substance infringe at least claims 1, 13, and 17 of the 663 Patent.

75. On information and belief, the Proposed ANDA Product and the drug substance in and used for the Proposed ANDA Product infringe at least claim 1 of the 663 Patent because they

contain crystalline Form B of apalutamide that is characterized as having at least one of an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in FIG. 2 of the 663 Patent or an X-ray powder diffraction (XRPD) pattern with characteristic peaks at $12.1\pm0.1^\circ$ 2-Theta, $16.0\pm0.1^\circ$ 2-Theta, $16.7\pm0.1^\circ$ 2-Theta, $20.1\pm0.1^\circ$ 2-Theta, $20.3\pm0.1^\circ$ 2-Theta.

76. On information and belief, the Proposed ANDA Product and the drug substance in and used for the Proposed ANDA Product infringe at least claim 13 of the 663 Patent because they are a pharmaceutical composition comprising apalutamide and at least one additional ingredient selected from pharmaceutically acceptable carriers, diluents and excipients, in which the apalutamide in the composition comprises the crystalline Form B that is characterized as having at least one of an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in FIG. 2 of the 663 Patent or an X-ray powder diffraction (XRPD) pattern with characteristic peaks at $12.1\pm0.1^\circ$ 2-Theta, $16.0\pm0.1^\circ$ 2-Theta, $16.7\pm0.1^\circ$ 2-Theta, $20.1\pm0.1^\circ$ 2-Theta, $20.3\pm0.1^\circ$ 2-Theta.

77. On information and belief, the use of the Proposed ANDA Product and the drug substance in and used for the Proposed ANDA Product will infringe at least claim 17 of the 663 Patent because physicians and/or patients will practice a method of treating prostate cancer in a mammal, specifically a patient, said method comprising administering, causing to be administered, or directing the administration of a pharmaceutical composition comprising apalutamide and at least one additional ingredient selected from pharmaceutically acceptable carriers, diluents and excipients, in which the apalutamide in the composition comprises the crystalline Form B that is characterized as having at least one of an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in FIG. 2 of the 663 Patent or an X-ray powder diffraction (XRPD) pattern with

characteristic peaks at $12.1\pm0.1^\circ$ 2-Theta, $16.0\pm0.1^\circ$ 2-Theta, $16.7\pm0.1^\circ$ 2-Theta, $20.1\pm0.1^\circ$ 2-Theta, $20.3\pm0.1^\circ$ 2-Theta to the patient in need of such treatment.

78. On information and belief, Defendants will induce infringement of at least claim 17 of the 663 Patent by actively inducing the use of the Proposed ANDA Product to practice a method of treating prostate cancer in a mammal, specifically a patient, said method comprising administering, causing to be administered, or directing the administration of a pharmaceutical composition comprising apalutamide and at least one additional ingredient selected from pharmaceutically acceptable carriers, diluents and excipients, in which the apalutamide in the composition comprises the crystalline Form B that is characterized as having at least one of an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in FIG. 2 of the 663 Patent or an X-ray powder diffraction (XRPD) pattern with characteristic peaks at $12.1\pm0.1^\circ$ 2-Theta, $16.0\pm0.1^\circ$ 2-Theta, $16.7\pm0.1^\circ$ 2-Theta, $20.1\pm0.1^\circ$ 2-Theta, $20.3\pm0.1^\circ$ 2-Theta to the patient in need of such treatment.

79. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 663 Patent, including at least claims 1, 13, and 17, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 663 Patent, including at least claims 1, 13, and 17, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

80. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 663 Patent. The Notice Letter did not include a detailed and

supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 663 Patent.

81. On information and belief, Defendants have actual knowledge of the 663 Patent, at least as shown by the Notice Letter.

82. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 663 Patent, including at least claims 1, 13, and 17, by submitting or causing to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 663 Patent.

83. On information and belief, the Proposed ANDA Product and its use, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of the 663 Patent, including at least claims 1, 13, and 17, under at least one of 35 U.S.C. § 271(a), (b), or (c).

84. On information and belief, the manufacture, use, import, offer to sell, or sale of the Proposed ANDA Product will directly infringe the claims of the 663 Patent, including at least claims 1, 13, and 17.

85. On information and belief, physicians and/or patients will directly infringe the claims of the 663 Patent, including at least claims 1, 13, and 17, by the use of the Proposed ANDA Product upon approval.

86. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 663 Patent, including at least claims 1, 13, and 17, for the pecuniary benefit of Defendants.

87. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 663 Patent, including at least claims 1, 13, and 17. On information and belief, Defendants will actively induce the infringement of the claims of the 663 Patent, including at least claims 1, 13, and 17.

88. On information and belief, the Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 663 Patent, including at least claims 1, 13, and 17. On information and belief, Defendants will thus contribute to the infringement of the claims of the 663 Patent, including at least claims 1, 13, and 17.

89. On information and belief, the actions described in this Complaint relating to the ANDA and the 663 Patent were done by and for the benefit of Defendants.

90. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

COUNT III – CLAIM FOR INFRINGEMENT OF THE 054 PATENT

91. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.

92. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 054 Patent, including at least claims 6 and 15.

93. On information and belief, the use of the Proposed ANDA Product will infringe at least claims 6 and 15 of the 054 Patent because physicians and/or patients will practice a method of treating non-metastatic castration-resistant prostate cancer in a male human, said method comprising administering, causing to be administered, or directing the administration of a therapeutically effective amount of an anti-androgen to a male human in need of such treatment,

wherein the anti-androgen is apalutamide that is administered orally to the male human at a dose of about 240 mg per day.

94. On information and belief, Defendants will induce infringement of at least claims 6 and 15 of the 054 Patent by actively inducing the use of the Proposed ANDA Product to practice a method of treating non-metastatic castration-resistant prostate cancer in a male human, said method comprising administering, causing to be administered, or directing the administration of a therapeutically effective amount of an anti-androgen to a male human in need of such treatment, wherein the anti-androgen is apalutamide that is administered orally to the male human at a dose of about 240 mg per day.

95. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 054 Patent, including at least claims 6 and 15, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 054 Patent, including at least claims 6 and 15, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

96. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 054 Patent. The Notice Letter did not include a detailed and supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 054 Patent.

97. On information and belief, Defendants have actual knowledge of the 054 Patent, at least as shown by the Notice Letter.

98. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 054 Patent, including at least claims 6 and 15, by submitting or causing to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 054 Patent.

99. On information and belief, the use of the Proposed ANDA Product, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of the 054 Patent, including at least claims 6 and 15, under at least one of 35 U.S.C. § 271(a), (b), or (c).

100. On information and belief, physicians and/or patients will directly infringe the claims of the 054 Patent, including at least claims 6 and 15, by their use of the Proposed ANDA Product upon approval.

101. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 054 Patent, including at least claims 6 and 15, for the pecuniary benefit of Defendants.

102. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 054 Patent, including at least claims 6 and 15. On information and belief, Defendants will actively induce the infringement of the claims of the 054 Patent, including at least claims 6 and 15.

103. On information and belief, Defendants' Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 054 Patent, including at least claims

6 and 15. On information and belief, Defendants will thus contribute to the infringement of the claims of the 054 Patent, including at least claims 6 and 15.

104. On information and belief, the actions described in this Complaint relating to the ANDA and the 054 Patent were done by and for the benefit of Defendants.

105. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

**COUNT IV – CLAIM FOR INFRINGEMENT OF THE 314
PATENT**

106. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.

107. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 314 Patent, including at least claims 3 and 19.

108. On information and belief, the use of the Proposed ANDA Product will infringe at least claims 3 and 19 of the 314 Patent because physicians and/or patients will practice a method of treating a male human with non-metastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing the administration of an anti-androgen at a dose of about 240 mg per day to a male human in need of such treatment, wherein the anti-androgen is apalutamide, wherein said method further comprises administering a gonadotropin releasing hormone (GnRH) agonist.

109. Defendants will induce infringement of at least claims 3 and 19 of the 314 Patent by actively inducing the use of the Proposed ANDA Product to practice a method of treating a male human with non-metastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing the administration of an anti-androgen at a dose of about 240 mg per day to a male human in need of such treatment, wherein the anti-

androgen is apalutamide, wherein said method further comprises administering a gonadotropin releasing hormone (GnRH) agonist.

110. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 314 Patent, including at least claims 3 and 19, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 314 Patent, including at least claims 3 and 19, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

111. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 314 Patent. The Notice Letter did not include a detailed and supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 314 Patent.

112. On information and belief, Defendants have actual knowledge of the 314 Patent, at least as shown by the Notice Letter.

113. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 314 Patent, including at least claims 3 and 19, by submitting or causing to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 314 Patent.

114. On information and belief, the use of the Proposed ANDA Product, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of

the 314 Patent, including at least claims 3 and 19, under at least one of 35 U.S.C. § 271(a), (b), or (c).

115. On information and belief, physicians and/or patients will directly infringe the claims of the 314 Patent, including at least claims 3 and 19, by their use of the Proposed ANDA Product upon approval.

116. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 314 Patent, including at least claims 3 and 19, for the pecuniary benefit of Defendants.

117. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 314 Patent, including at least claims 3 and 19. On information and belief, Defendants will actively induce the infringement of the claims of the 314 Patent, including at least claims 3 and 19.

118. On information and belief, Defendants' Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 314 Patent, including at least claims 3 and 19. On information and belief, Defendants will thus contribute to the infringement of the claims of the 314 Patent, including at least claims 3 and 19.

119. On information and belief, the actions described in this Complaint relating to the ANDA and the 314 Patent were done by and for the benefit of Defendants.

120. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

**COUNT V – CLAIM FOR INFRINGEMENT OF THE 508
PATENT**

121. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.
122. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 508 Patent, including at least claims 1, 2, 5, and 7.
123. On information and belief, the use of the Proposed ANDA Product will infringe at least claims 1 and 2 of the 508 Patent because physicians and/or patients will practice a method of improving metastasis free survival in a male human with nonmetastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing the administration of, to said male human, an approved drug product comprising apalutamide in combination with androgen deprivation therapy, wherein the median metastasis free survival is about 40.5 months.
124. On information and belief, Defendants will induce infringement of at least claims 1 and 2 of the 508 Patent by actively inducing the use of the Proposed ANDA Product to practice a method of improving metastasis free survival in a male human with nonmetastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing the administration of, to said male human, an approved drug product comprising apalutamide in combination with androgen deprivation therapy, wherein the median metastasis free survival is about 40.5 months.
125. On information and belief, the use of the Proposed ANDA Product will infringe claims at least 5 and 7 of the 508 Patent because physicians and/or patients will practice a method of improving metastasis free survival in a male human with nonmetastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing

the administration of, to said male human, an approved drug product comprising apalutamide in combination with androgen deprivation therapy, wherein a drug product label for a reference listed drug for such approved drug product comprises metastasis free survival data, wherein the metastasis free survival data for apalutamide in combination with androgen deprivation therapy arm has a median of about 40.5 months.

126. On information and belief, Defendants will induce infringement of at least claims 5 and 7 of the 508 Patent by actively inducing the use of the Proposed ANDA Product as a method of improving metastasis free survival in a male human with nonmetastatic castration-resistant prostate cancer, said method comprising administering, causing to be administered, or directing the administration of, to said male human, an approved drug product comprising apalutamide in combination with androgen deprivation therapy, wherein a drug product label for a reference listed drug for such approved drug product comprises metastasis free survival data, wherein the metastasis free survival data for apalutamide in combination with androgen deprivation therapy arm has a median of about 40.5 months.

127. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 508 Patent, including at least claims 1, 2, 5, and 7, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 508 Patent, including at least claims 1, 2, 5, and 7, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

128. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 508 Patent. The Notice Letter did not include a detailed and supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 508 Patent.

129. On information and belief, Defendants have actual knowledge of the 508 Patent, at least as shown by the Notice Letter.

130. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 508 Patent, including at least claims 1, 2, 5, and 7, by submitting or causing to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 508 Patent.

131. On information and belief, the use of the Proposed ANDA Product, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of the 508 Patent, including at least claims 1, 2, 5, and 7, under at least one of 35 U.S.C. § 271(a), (b), or (c).

132. On information and belief, physicians and/or patients will directly infringe the claims of the 508 Patent, including at least claims 1, 2, 5, and 7, by their use of the Proposed ANDA Product upon approval.

133. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 508 Patent, including at least claims 1, 2, 5, and 7, for the pecuniary benefit of Defendants.

134. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 508 Patent, including at least claims 1, 2, 5, and 7. On information and belief, Defendants will actively induce the infringement of the claims of the 508 Patent, including at least claims 1, 2, 5, and 7.

135. On information and belief, Defendants' Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 508 Patent, including at least claims 1, 2, 5, and 7. On information and belief, Defendants will thus contribute to the infringement of the claims of the 508 Patent, including at least claims 1, 2, 5, and 7.

136. On information and belief, the actions described in this Complaint relating to the ANDA and the 508 Patent were done by and for the benefit of Defendants.

137. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

COUNT VI – CLAIM FOR INFRINGEMENT OF THE 888 PATENT

138. Plaintiffs re-allege each of the foregoing paragraphs as if fully set forth herein.

139. An actual controversy exists between the parties as to whether Defendants' proposed sale of the Proposed ANDA Product infringes the claims of the 888 Patent, including at least claims 1 and 8.

140. On information and belief, the use of the Proposed ANDA Product will infringe at least claims 1 and 8 of the 888 Patent because physicians and/or patients will practice a method of treating non-metastatic castration-resistant prostate cancer in a male human, said method comprising administering, causing to be administered, or directing the administration of an anti-androgen at a dose of about 240 mg per day to a male human in need of such treatment, wherein the anti-androgen is apalutamide and wherein said method further comprises orchietomy.

141. On information and belief, Defendants will induce infringement of at least claims 1 and 8 of the 888 Patent by actively inducing the use of the Proposed ANDA Product to practice a method of treating non-metastatic castration-resistant prostate cancer in a male human, said method comprising administering, causing to be administered, or directing the administration of an anti-androgen at a dose of about 240 mg per day to a male human in need of such treatment, wherein the anti-androgen is apalutamide and wherein said method further comprises orchiectomy.

142. On information and belief, if the FDA approves the ANDA, Defendants will sell or offer to sell the Proposed ANDA Product specifically labeled for use in practicing the claims of the 888 Patent, including at least claims 1 and 8, wherein the Proposed ANDA Product is a material part of the claimed invention, wherein Defendants know that physicians will prescribe and patients will use the Proposed ANDA Product in accordance with the instructions or label provided by Defendants in practicing the claims of the 888 Patent, including at least claims 1 and 8, and wherein the Proposed ANDA Product is not a staple article or commodity of commerce suitable for substantial non-infringing use.

143. The Notice Letter purports to include a Notice of Certification for the ANDA under 37 C.F.R. § 314.95(c)(6) as to the 888 Patent. The Notice Letter did not include a detailed and supported statement of allegations of invalidity, unenforceability, or non-infringement for every claim of the 888 Patent.

144. On information and belief, Defendants have actual knowledge of the 888 Patent, at least as shown by the Notice Letter.

145. On information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed the claims of the 888 Patent, including at least claims 1 and 8, by submitting or causing

to be submitted to the FDA, the ANDA seeking approval to manufacture, use, import, offer to sell or sell the Proposed ANDA Product before the expiration date of the 888 Patent.

146. On information and belief, the use of the Proposed ANDA Product, if approved and marketed, will infringe, either literally or under the doctrine of equivalents, at least one claim of the 888 Patent, including at least claims 1 and 8, under at least one of 35 U.S.C. § 271(a), (b), or (c).

147. On information and belief, physicians and/or patients will directly infringe the claims of the 888 Patent, including at least claims 1 and 8, by their use of the Proposed ANDA Product upon approval.

148. On information and belief, upon approval, Defendants will take active steps to encourage the use of the Proposed ANDA Product by physicians and/or patients with the knowledge and intent that the Proposed ANDA Product will be used by physicians and/or patients, in a manner that infringes the claims of the 888 Patent, including at least claims 1 and 8, for the pecuniary benefit of Defendants.

149. On information and belief, Defendants specifically intend the Proposed ANDA Product to be used in a manner that infringes the claims of the 888 Patent, including at least claims 1 and 8. On information and belief, Defendants will actively induce the infringement of the claims of the 888 Patent, including at least claims 1 and 8.

150. On information and belief, Defendants' Proposed ANDA Product is specifically designed for use in a manner that infringes the claims of the 888 Patent, including at least claims 1 and 8. On information and belief, Defendants will thus contribute to the infringement of the claims of the 888 Patent, including at least claims 1 and 8.

151. On information and belief, the actions described in this Complaint relating to the ANDA and the 888 Patent were done by and for the benefit of Defendants.

152. Plaintiffs will be irreparably harmed by these infringing activities unless those activities are enjoined by this Court. Plaintiffs do not have an adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that the Court enter judgment in their favor and against Defendants on the patent infringement claims set forth above and respectfully request that this Court:

A. Enter judgment under 35 U.S.C. § 271(e)(2)(A) that Defendants have infringed one or more claims of each of the Patents-In-Suit through the submission of the ANDA to the FDA to obtain approval to manufacture, use, import, offer to sell, and sell the Proposed ANDA Product in the United States before the expiration of the Patents-In-Suit;

B. Enter a declaratory judgment that pursuant to 35 U.S.C. § 271(a), (b), and/or (c), the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States of the Proposed ANDA Product, prior to the expiration of the Patents-In-Suit, would constitute infringement of one or more claims of each of the Patents-In-Suit under 35 U.S.C. § 271 (a), (b), and/or (c);

C. Order that pursuant to 35 U.S.C. § 271(e)(4)(A) the effective date of any approval of the ANDA be a date that is not earlier than the expiration dates of the Patents-In-Suit, or such later date as the Court may determine;

D. Order that Defendants, their officers, agents, servants, and employees, and those persons in active concert or participation with Defendants, are preliminarily and permanently enjoined from commercially manufacturing, using, importing, offering for sale, and selling the

Proposed ANDA Product, and any other product that infringes or induces or contributes to the infringement of the Patents-In-Suit, prior to the expiration of the Patents-In-Suit, or such later date as the Court may determine;

E. If Defendants engage in the commercial manufacture, use, offer for sale, sale, and/or importation into the United States of the Proposed ANDA Product prior to the expiration of the Patents-In-Suit, a judgment awarding damages to Plaintiffs resulting from such infringement together with interest;

F. Declare this to be an exceptional case under 35 U.S.C. §§ 285 and 271(e)(4) and award Plaintiffs their costs, expenses, and disbursements in this action, including reasonable attorney fees; and

G. Award such further and other relief as this Court deems proper and just.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

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