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ARIAD Pharmaceuticals Inc.

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

TAKEDA PHARMACEUTICALS AMERICA, INC., TAKEDA PHARMACEUTICALS U.S.A., INC., and ARIAD PHARMACEUTICALS INC.,

Plaintiffs,

v.

APOTEX, INC.,

Defendant.

Civil Action No. 21-12998

FIRST AMENDED COMPLAINT

(Filed Electronically)

Plaintiffs Takeda Pharmaceuticals America, Inc. ("TPA"), Takeda Pharmaceuticals U.S.A., Inc. ("TPUSA"), and ARIAD Pharmaceuticals Inc. ("Ariad") (collectively, "Plaintiffs"), by their attorneys, for their complaint against Apotex, Inc. ("Apotex") allege as follows:

NATURE OF THE ACTION

1. This is a civil action for infringement of United States Patent Nos. 9,493,470 (the "'470 patent"), 11,192,897 (the "'897 patent"), 11,192,895 (the "'895 patent") (collectively the "Patents-in-Suit") under the patent laws of the United States, 35 U.S.C. § 100, *et seq.* This action arises from Apotex's submission of Abbreviated New Drug Application ("ANDA") No. 215893 ("the Apotex ANDA") to the United States Food and Drug Administration ("FDA") seeking approval to manufacture, use, import, distribute, offer to sell, and/or sell generic versions of Plaintiffs' 15 mg and 45 mg ICLUSIG® drug product ("the Apotex ANDA Product") prior to the expiration of the Patents-in-Suit.

THE PARTIES

2. TPA is a corporation organized and existing under the laws of the State of Delaware, having an office and place of business at 95 Hayden Avenue, Lexington, MA 02421.

3. TPUSA is a corporation organized and existing under the laws of the State of Delaware, having an office and place of business at 95 Hayden Avenue, Lexington, MA 02421.

4. Ariad is a corporation organized and existing under the laws of the State of Delaware, having an office and place of business at 40 Lansdowne Street, Cambridge, MA 02139.

5. On information and belief, defendant Apotex, Inc. is a corporation organized and existing under the laws of Canada, having a principal place of business at 150 Signet Drive, Toronto, Ontario, Canada M9L 1T9.

THE PATENTS-IN-SUIT

6. On November 15, 2016, the United States Patent and Trademark Office duly and lawfully issued the ’470 patent, entitled “Crystalline forms of 3-(imidazo[1,2-B] pyridazin-3-ylethynyl)-4-methyl-N-{4-[(4-methylpiperazin-1-yl) methyl]-3-(trifluoromethyl)phenyl}benzamide and its mono hydrochloride salt” to Ariad as assignee of inventors Christopher K. Murray, Leonard W. Rozamus, John J. Chaber, and Pradeep Sharma. A copy of the ’470 patent is attached as Exhibit A.

7. On December 7, 2021, the United States Patent and Trademark Office duly and lawfully issued the ’897 patent, entitled “Crystalline forms of 3-(imidazo[1,2-B] pyridazin-3-ylethynyl)-4-methyl-N-{4-[(4-methylpiperazin-1-yl) methyl]-3-(trifluoromethyl)phenyl}benzamide and its mono hydrochloride salt” to Ariad as assignee of inventors Christopher K. Murray, Leonard W. Rozamus, John J. Chaber, and Pradeep Sharma. A copy of the ’895 patent is attached as Exhibit B.

8. On December 7, 2021, the United States Patent and Trademark Office duly and lawfully issued the ’895 patent, entitled “Crystalline forms of 3-(imidazo[1,2-B] pyridazin-3-ylethynyl)-4-methyl-N-{4-[(4-methylpiperazin-1-yl) methyl]-3-(trifluoromethyl)phenyl}benzamide and its mono hydrochloride salt” to Ariad as assignee of inventors Christopher K. Murray, Leonard W. Rozamus, John J. Chaber, and Pradeep Sharma. A copy of the ’895 patent is attached as Exhibit C.

THE ICLUSIG® DRUG PRODUCT

9. TPUSA holds approved New Drug Application No. 203469 for ponatinib hydrochloride tablets, which are prescribed and sold under the trademark ICLUSIG®. ICLUSIG® is indicated for the treatment of adult patients with (1) chronic phase chronic myeloid leukemia with resistance or intolerance to at least two prior kinase inhibitors, (2) accelerated phase or blast phase chronic myeloid leukemia or Philadelphia chromosome positive acute lymphoblastic leukemia for all whom no other kinase inhibitors are indicated, and (3) T315I-positive chronic myeloid leukemia (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia.

10. The claims of the Patents-in-Suit cover, *inter alia*, crystalline forms of ponatinib hydrochloride, compositions comprising crystalline forms of ponatinib hydrochloride, and methods of treating chronic myeloid leukemia, or Philadelphia chromosome-positive acute lymphoblastic leukemia.

11. Pursuant to 21 U.S.C. § 355(b)(1), and attendant FDA regulations, the '470 patent is listed in the FDA publication "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), with respect to ICLUSIG®.

12. Pursuant to the FDA-approved labeling, ICLUSIG® instructs and encourages physicians, pharmacists, other healthcare workers, and patients to administer ICLUSIG® for the treatment of, *inter alia*, adult patients with chronic phase chronic myeloid leukemia with resistance or intolerance to at least two prior kinase inhibitors.

13. Pursuant to the FDA-approved labeling, ICLUSIG® instructs and encourages physicians, pharmacists, other healthcare workers, and patients to administer ICLUSIG® for the treatment of, *inter alia*, adult patients with accelerated phase or blast phase

chronic myeloid leukemia or Philadelphia chromosome positive acute lymphoblastic leukemia for all whom no other kinase inhibitors are indicated.

14. Pursuant to the FDA-approved labeling, ICLUSIG® instructs and encourages physicians, pharmacists, other healthcare workers, and patients to administer ICLUSIG® for the treatment of, *inter alia*, adult patients with T315I-positive chronic myeloid leukemia (chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia.

JURISDICTION AND VENUE

15. This action arises under the patent laws of the United States, 35 U.S.C. §§ 100, *et seq.*, and this Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

16. On information and belief, Apotex is in the business of, among other things, manufacturing, marketing, importing, offering for sale, and selling pharmaceutical products, including generic drug products, throughout the United States, including in this Judicial District. On information and belief, this Judicial District will be a destination for the generic drug products described in Apotex's ANDA. On information and belief, Apotex prepares and/or aids in the preparation and submission of ANDAs to the FDA.

17. This Court has personal jurisdiction over Apotex because Apotex has purposefully availed itself of the rights and benefits of New Jersey law by engaging in systematic and continuous contact with the State of New Jersey. On information and belief, Apotex regularly and continuously transacts business within New Jersey, including by making pharmaceutical products for sale in New Jersey and selling pharmaceutical products in New Jersey. On information and belief, Apotex derives substantial revenue from the sale of those products in New Jersey and has availed itself of the privilege of conducting business within New

Jersey. On information and belief, Apotex derives substantial revenue from selling generic pharmaceutical products throughout the United States, including in this Judicial District. For example, upon information and belief, Apotex states on their website that they "export to more than 115 countries and territories, and operate in more than 45 countries, including a significant presence in the US, Mexico and India where we continue to invest." Apotex Website, https://www1.apotex.com/us/about-us/about-apotex (last visited June 16, 2021).

18. This Court has personal jurisdiction over Apotex because, *inter alia*, Apotex has committed an act of patent infringement under 35 U.S.C. § 271(e)(2) and intends a future course of conduct that includes acts of patent infringement in New Jersey. These acts have led and will lead to foreseeable harm and injury to Plaintiffs in New Jersey. For example, on information and belief, following approval of the Apotex ANDA, Apotex will make, use, import, sell, and/or offer for sale the Apotex ANDA Product in the United States, including in New Jersey, prior to the expiration of the Patents-in-Suit.

19. This Court also has personal jurisdiction over Apotex because, *inter alia*, Apotex has purposefully availed itself of the rights and benefits of New Jersey law by engaging in systematic and continuous contacts with the State of New Jersey.

20. On information and belief, Apotex has previously invoked, stipulated, and/or consented to personal jurisdiction in this Judicial District in numerous prior patent cases.

21. Apotex has previously been sued in this Judicial District and has availed itself of New Jersey courts through the assertion of counterclaims in suits brought in New Jersey and has not challenged personal jurisdiction. *See, e.g., Celgene Corporation v. Apotex Inc.*, Civil Action No. 19-5806 (ES)(MAH) (D.N.J.); *Celgene Corporation v. Apotex Inc.*, Civil Action No. 18-16395 (ES)(MAH) (D.N.J.); *Celgene Corporation v. Hetero Labs Limited, et al.*, Civil Action

No. 17-3387 (ES)(MAH) (D.N.J.); *Mitsubishi Tanabe Pharma Corporation, et al. v. Apotex Inc., et al.*, Civil Action No. 17-5278 (PGS)(DEA) (D.N.J.); *AstraZeneca AB, et al. v. Apotex Corp., et al.*, Civil Action No. 15-8492 (FLW)(DEA) (D.N.J.); *Bausch & Lomb Inc., et al. v. Apotex Inc., et al.*, Civil Action No. 15-3879 (NLH)(JS) (D.N.J.); *Novartis Pharm. Corp. v. Apotex Inc., et al.*, Civil Action No. 15-3634 (SDW)(LDW) (D.N.J.); *Merck Sharp & Dohme Corp. v. Apotex Inc., et al.*, Civil Action No. 15-2384 (PGS)(TJB) (D.N.J.); *Patheon Softgels Inc., et al. v. Apotex Inc., et al.*, Civil Action No. 17-13819 (MAS)(LHG) (D.N.J.); *Dexcel Pharma Technologies Ltd., et al. v. Apotex Corp., et al.*, Civil Action No. 17-02423 (SDW)(LDW) (D.N.J.); *Boehringer Ingelheim Pharmaceuticals, Inc., et al. v. Apotex Inc., et al.*, Civil Action No. 18-11350 (MAS)(LHG) (D.N.J.).

22. Apotex has further availed itself of the jurisdiction of this Court by initiating litigation in this Judicial District. *See, e.g.*, *Apotex Inc. v. Shire LLC*, Civil Action No. 08-3598 (SRC)(MAS) (D.N.J.); *Apotex Inc., et al. v. Pharmaceutical Resources, Inc.*, Civil Action No. 06-1153 (JLL)(MF) (D.N.J.).

23. In the alternative, this Court has personal jurisdiction over Apotex because the requirements of Federal Rule of Civil Procedure 4(k)(2)(A) are met as (a) Plaintiffs' claims arise under federal law; (b) Apotex is a foreign defendant not subject to general personal jurisdiction in the courts of any state; and (c) Apotex has sufficient contacts with the United States as a whole, including, but not limited to, preparing and submitting an ANDA to the FDA and/or manufacturing and/or selling pharmaceutical products distributed throughout the United States, such that this Court's exercise of jurisdiction over Apotex satisfies due process.

24. Apotex has not contested personal jurisdiction in this case.

25. Venue is proper in this Judicial District pursuant to 28 U.S.C. §§ 1391 and/or 1400(b), because Apotex is incorporated in Canada and may be sued in any judicial district. Apotex has not contested venue in this case.

APOTEX INFRINGING ANDA SUBMISSION

26. On or about May 17, 2021, Plaintiffs received from Apotex a letter dated May 14, 2021 ("Apotex Letter"), stating that Apotex had submitted the Apotex ANDA to the FDA seeking approval to commercially manufacture, use, sell, offer for sale, or import the Apotex ANDA Product before the expiration of the Patents-in-Suit.[1]

27. On information and belief, in connection with the submission of its ANDA as described above, Apotex provided a written certification to the FDA as called for by Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(j)(2)(A)(vii)(IV).

28. On information and belief, in connection with the submission of its ANDA as described above, Apotex provided a written certification to the FDA as called for by Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355(j)(2)(A)(vii)(III), wherein Apotex does not seek FDA approval of Apotex's ANDA until after the Orange Book Patents, U.S. Patent Nos. 8,114,874 and 9,029,533, have expired.

29. On information and belief, following FDA approval of Apotex's ANDA, Apotex will make, use, offer for sale, or sell Apotex's ANDA Product throughout the United States, or import such generic products into the United States.

30. The Apotex ANDA Product is intended to be a generic version of ICLUSIG®.

[1] The expiration date for the Patents-in-Suit is December 12, 2033.

31. The Apotex Letter alleges, *inter alia*, that the claims of the '470 patent are invalid and/or will not be infringed by the activities described in Apotex's ANDA. The Apotex Letter does not assert any non-infringement defenses that Apotex makes and/or uses a different crystalline form of ponatinib hydrochloride than claimed in one or more claims of the '470 patent. Nor does the Apotex Letter assert any non-infringement defenses based on the proposed indication for the Apotex ANDA Product. Notwithstanding Apotex's allegations in the Apotex Letter, on information and belief, discovery will show that the Apotex ANDA Product infringes one or more claims of the Patents-in-Suit.

32. This action was commenced before the expiration of 45 days from the date Plaintiffs received the Apotex Letter. This First Amended Complaint is being filed pursuant to the Court's Pretrial Scheduling Order. D.I. 25.

COUNT I
Infringement of U.S. Patent No. 9,493,470 by Apotex

33. Plaintiffs repeat and reallege the preceding paragraphs above as if fully set forth herein.

34. By submitting its ANDA No. 215893 for the purpose of obtaining approval to engage in the commercial manufacture, use, sale, offer for sale, or importation into the United States of the Apotex ANDA Product before the expiration of the '470 patent, Apotex committed an act of infringement under 35 U.S.C. § 271(e)(2).

35. On information and belief, the Apotex ANDA Product is a pharmaceutical composition that includes crystalline forms of ponatinib hydrochloride recited in one or more claims of the '470 patent (e.g., claims 1-7, 10, and 12-15) and Apotex seeks FDA approval for its ANDA Product for one or more claimed methods of treatment (e.g., claims 8-9, 11, and 16-17), and discovery will show that if Apotex commercially makes, uses, offers to sell, or sells the

Apotex ANDA Product within the United States, or imports the Apotex ANDA Product into the United States, or induces or contributes to any such conduct during the term of the '470 patent, it would further infringe one or more claims of the '470 patent under 35 U.S.C. §§ 271(a), (b), and/or (c).

36. Claim 1 of the '470 patent recites:

> Crystalline Form A of ponatinib hydrochloride characterized by an x-ray powder diffraction pattern comprising at least five 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 16.4, 19.3, 21.8, 23.8, and 26.1.

37. On information and belief, the Apotex ANDA Product will contain the crystalline Form A of ponatinib hydrochloride.

38. On information and belief, the crystalline Form A of ponatinib hydrochloride in the Apotex ANDA Product is characterized by an x-ray powder diffraction pattern comprising at least five 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 16.4, 19.3, 21.8, 23.8, and 26.1

39. Claim 8 of the '470 patent recites:

> A method for treating chronic myeloid leukemia or Philadelphia chromosome-positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition [comprising crystalline Form A ponatinib hydrochloride according to claim 1 and at least one pharmaceutically acceptable carrier, vehicle or excipient].

40. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating chronic myeloid leukemia or Philadelphia chromosome-positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition. On further information and belief, the pharmaceutical composition of the Apotex

ANDA Product comprises crystalline Form A ponatinib hydrochloride according to claim 1 of the ’470 patent and at least one pharmaceutically acceptable carrier, vehicle or excipient.

41. Unless enjoined by this Court, upon FDA approval of Apotex’s ANDA, Apotex will infringe one or more claims of the ’470 patent under 35 U.S.C. § 271(a) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States.

42. Unless enjoined by this Court, upon FDA approval of Apotex’s ANDA, Apotex will induce infringement of one or more claims of the ’470 patent under 35 U.S.C. § 271(b) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, upon FDA approval of Apotex’s ANDA, Apotex will intentionally encourage acts of direct infringement with knowledge of the ’470 patent and knowledge that its acts are encouraging infringement.

43. Unless enjoined by this Court, upon FDA approval of Apotex’s ANDA, Apotex will contributorily infringe one or more claims of the ’470 patent under 35 U.S.C. § 271(c) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, Apotex has had and continues to have knowledge that the Apotex ANDA Product is especially adapted for a use that infringes one or more claims of the ’470 patent and that there is no substantial non-infringing use for the Apotex ANDA Product.

44. Apotex has had knowledge of the ’470 patent since at least the date it submitted the Apotex ANDA.

45. Plaintiffs will be substantially and irreparably harmed if Apotex is not enjoined from infringing the ’470 patent. Plaintiffs do not have an adequate remedy at law.

46. This case is an exceptional one, and Plaintiffs are entitled to an award of its reasonable attorneys' fees under 35 U.S.C. § 285.

COUNT II
Infringement of U.S. Patent No. 11,192,897 by Apotex

47. Plaintiffs repeat and reallege the preceding paragraphs above as if fully set forth herein.

48. By submitting its ANDA No. 215893 for the purpose of obtaining approval to engage in the commercial manufacture, use, sale, offer for sale, or importation into the United States of the Apotex ANDA Product before the expiration of the '897 patent, Apotex committed an act of infringement under 35 U.S.C. § 271(e)(2).

49. On information and belief, the Apotex ANDA Product is a pharmaceutical composition that includes crystalline forms of ponatinib hydrochloride recited in one or more claims of the '897 patent (e.g., claims 1-14 of the '897 patent) and Apotex seeks FDA approval for its ANDA Product for one or more claimed methods of treatment (e.g., claims 15-23 of the '897 patent), and discovery will show that if Apotex commercially makes, uses, offers to sell, or sells the Apotex ANDA Product within the United States, or imports the Apotex ANDA Product into the United States, or induces or contributes to any such conduct during the term of the '897 patent, it would further infringe one or more claims of the '897 patent under 35 U.S.C. §§ 271(a), (b), and/or (c).

50. Claim 1 of the '897 patent recites:

> A crystalline form of ponatinib hydrochloride characterized by an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1.

51. On information and belief, the Apotex ANDA Product will contain the crystalline form of ponatinib hydrochloride.

52. On information and belief, the crystalline form of ponatinib hydrochloride in the Apotex ANDA Product is characterized by an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1.

53. Claim 5 of the ’897 patent recites:

> A crystalline form of ponatinib hydrochloride, wherein the crystalline form
>
> (a) does not change as measured by XRPD and undergoes no apparent degradation as measured by HPLC after exposure to 70 °C for up to 72 hours;
> (b) does not change as measured by XRPD and undergoes no apparent degradation as measured by HPLC after exposure to 220 °C for 5 minutes;
> (c) does not change as measured by XPRD and the DVS isotherm does not change after exposure to DVS cycling of 0-95-0% RH followed by 0-45% RH; and/or
> (d) does not change as measured by XPRD and DSC after exposure to 75% RH for 6 days.

54. On information and belief, the crystalline form of ponatinib hydrochloride in the Apotex ANDA Product does not change as measured by XPRD according to claim 5 of the ’897 patent.

55. Claim 11 of the ’897 patent recites:

> A crystalline form of ponatinib hydrochloride having an onset melting temperature of 262 °C to 264 °C.

56. On information and belief, the crystalline form of ponatinib hydrochloride in the Apotex ANDA Product has an onset melting temperature of 262 °C to 264 °C.

57. Claim 13 of the ’897 patent recites:

> A pharmaceutical composition comprising at least two crystalline forms of ponatinib hydrochloride and a pharmaceutically acceptable carrier.

58. On information and belief, the Apotex ANDA Product will contain a pharmaceutical composition comprising at least two crystalline forms of ponatinib hydrochloride and a pharmaceutically acceptable carrier.

59. Claim 15 of the '897 patent recites:

> A method for treating chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the crystalline form of ponatinib hydrochloride according to claim 1 or the pharmaceutical composition according to claim 13.

60. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of crystalline form of ponatinib hydrochloride according to claim 15 of the '897 patent.

61. Claim 22 of the '897 patent recites:

> A method for treating Philadelphia chromosome positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of the crystalline form of ponatinib hydrochloride according to claim 1 or the pharmaceutical composition according to claim 13.

62. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating Philadelphia chromosome positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of crystalline form of ponatinib hydrochloride according to claim 22 of the '897 patent.

63. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will infringe one or more claims of the '897 patent under 35 U.S.C. § 271(a) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States.

64. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will induce infringement of one or more claims of the '897 patent under 35 U.S.C. § 271(b) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, upon FDA approval of Apotex's ANDA, Apotex will intentionally encourage acts of direct infringement with knowledge of the '897 patent and knowledge that its acts are encouraging infringement.

65. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will contributorily infringe one or more claims of the '897 patent under 35 U.S.C. § 271(c) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, Apotex has had and continues to have knowledge that the Apotex ANDA Product is especially adapted for a use that infringes one or more claims of the '897 patent and that there is no substantial non-infringing use for the Apotex ANDA Product.

66. Apotex has had knowledge of the claims of the '897 patent since at least the date Plaintiffs disclosed the asserted claims for the Patents-in-Suit including from the application that would issue as the '897 patent pursuant to Local Patent Rule 3.6(b) on November 19, 2021.

67. Plaintiffs will be substantially and irreparably harmed if Apotex is not enjoined from infringing the '897 patent. Plaintiffs do not have an adequate remedy at law.

68. This case is an exceptional one, and Plaintiffs are entitled to an award of its reasonable attorneys' fees under 35 U.S.C. § 285.

COUNT III
Infringement of U.S. Patent No. 11,192,895 by Apotex

69. Plaintiffs repeat and reallege the preceding paragraphs above as if fully set forth herein.

70. By submitting its ANDA No. 215893 for the purpose of obtaining approval to engage in the commercial manufacture, use, sale, offer for sale, or importation into the United States of the Apotex ANDA Product before the expiration of the '895 patent, Apotex committed an act of infringement under 35 U.S.C. § 271(e)(2).

71. On information and belief, Apotex seeks FDA approval for its ANDA Product for one or more claimed methods of treatment (e.g., claims 1-24 of the '895 patent), and discovery will show that if Apotex commercially makes, uses, offers to sell, or sells the Apotex ANDA Product within the United States, or imports the Apotex ANDA Product into the United States, or induces or contributes to any such conduct during the term of the '895 patent, it would further infringe one or more claims of the '895 patent under 35 U.S.C. §§ 271(a), (b), and/or (c).

72. Claim 1 of the '895 patent recites:

> A method for treating chronic phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising at least one crystalline form of ponatinib hydrochloride characterized by:
>
> a) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1;
>
> b) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 15.4, 16.2, 17.4, 18.0, 20.4, 23.2, 24.4, 26.1, and 26.9;

> c) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 17.4, 18.0, 20.6, 22.0, 23.0, 25.5, 26.5, 27.4, 28.4, and 29.0;
>
> d) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.2, 10.1, 10.9, 14.9, 16.0, 16.3, 16.8, 17.7, 18.7, 20.2, 22.9, 24.0, 25.6, 26.7, and 28.5;
>
> e) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl1 + HCl4 (GRP1.1);
>
> f) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 7.9, 8.7, 9.7, 11.4, 15.6, 16.5, and 25.8;
>
> g) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl5b (VDS28.2);
>
> h) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.0, 10.2, 10.9, 11.8, 14.1, 15.4, 16.3, 19.9, 22.3, 23.7, 25.0, and 28.2;
>
> i) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.0, 13.3, 16.4, 20.7, 22.2, 23.9, 25.5, and 29.1; or
>
> j) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.4, 13.5, 17.4, 18.5, 20.7, 23.9, and 28.3.

73. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating chronic phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition. On further information and belief, the pharmaceutical composition of the Apotex ANDA Product comprises at least one crystalline form of ponatinib hydrochloride according to claim 1 of the '895 patent.

74. Claim 7 of the '895 patent recites:

> A method for treating acute [sic accelerated] phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising at least one crystalline form of ponatinib hydrochloride

characterized by:

a) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1;

b) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 15.4, 16.2, 17.4, 18.0, 20.4, 23.2, 24.4, 26.1, and 26.9;

c) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 17.4, 18.0, 20.6, 22.0, 23.0, 25.5, 26.5, 27.4, 28.4, and 29.0;

d) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.2, 10.1, 10.9, 14.9, 16.0, 16.3, 16.8, 17.7, 18.7, 20.2, 22.9, 24.0, 25.6, 26.7, and 28.5

e) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl1 + HCl4 (GRP1.1);

f) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 7.9, 8.7, 9.7, 11.4, 15.6, 16.5, and 25.8;

g) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl5b (VDS28.2);

h) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.0, 10.2, 10.9, 11.8, 14.1, 15.4, 16.3, 19.9, 22.3, 23.7, 25.0, and 28.2;

i) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.0, 13.3, 16.4, 20.7, 22.2, 23.9, 25.5, and 29.1; or

j) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.4, 13.5, 17.4, 18.5, 20.7, 23.9, and 28.3.

75. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating accelerated phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition. On further information and

belief, the pharmaceutical composition of the Apotex ANDA Product comprises crystalline form of ponatinib hydrochloride according to claim 7 of the '895 patent.

76. Claim 13 of the '895 patent recites:

> A method of treating blast phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising at least one crystalline form of ponatinib hydrochloride characterized by:
>
> a) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1;
>
> b) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 15.4, 16.2, 17.4, 18.0, 20.4, 23.2, 24.4, 26.1, and 26.9;
>
> c) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 17.4, 18.0, 20.6, 22.0, 23.0, 25.5, 26.5, 27.4, 28.4, and 29.0;
>
> d) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.2, 10.1, 10.9, 14.9, 16.0, 16.3, 16.8, 17.7, 18.7, 20.2, 22.9, 24.0, 25.6, 26.7, and 28.5;
>
> e) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl1 + HCl4 (GRP1.1);
>
> f) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 7.9, 8.7, 9.7, 11.4, 15.6, 16.5, and 25.8;
>
> g) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl5b (VDS28.2);
>
> h) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.0, 10.2, 10.9, 11.8, 14.1, 15.4, 16.3, 19.9, 22.3, 23.7, 25.0, and 28.2;
>
> i) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.0, 13.3, 16.4, 20.7, 22.2, 23.9, 25.5, and 29.1; or

> j) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.4, 13.5, 17.4, 18.5, 20.7, 23.9, and 28.3.

77. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of treating blast phase chronic myeloid leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition. On further information and belief, the pharmaceutical composition of the Apotex ANDA Product comprises crystalline form of ponatinib hydrochloride according to claim 13 of the '895 patent**.**

78. Claim 19 of the '895 patent recites:

> A method of treating Philadelphia chromosome positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising at least one crystalline form of ponatinib hydrochloride characterized by:
>
> a) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 5.9, 7.1, 10.0, 12.5, 13.6, 14.1, 15.0, 16.4, 17.7, 18.6, 19.3, 20.4, 21.8, 22.3, 23.8, 24.9, 26.1, 27.0, 28.4, 30.3, 31.7, and 35.1;
>
> b) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 15.4, 16.2, 17.4, 18.0, 20.4, 23.2, 24.4, 26.1, and 26.9;
>
> c) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 3.1, 6.5, 12.4, 13.8, 17.4, 18.0, 20.6, 22.0, 23.0, 25.5, 26.5, 27.4, 28.4, and 29.0;
>
> d) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.2, 10.1, 10.9, 14.9, 16.0, 16.3, 16.8, 17.7, 18.7, 20.2, 22.9, 24.0, 25.6, 26.7, and 28.5;
>
> e) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl1 + HCl4 (GRP1.1);
>
> f) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 7.9, 8.7, 9.7, 11.4, 15.6, 16.5, and 25.8;

g) an x-ray powder diffraction pattern substantially as shown in FIG. 41 labelled HCl5b (VDS28.2);

h) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 8.0, 10.2, 10.9, 11.8, 14.1, 15.4, 16.3, 19.9, 22.3, 23.7, 25.0, and 28.2;

i) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.0, 13.3, 16.4, 20.7, 22.2, 23.9, 25.5, and 29.1; or

j) an x-ray powder diffraction pattern comprising at least three 2θ values (±0.3) chosen from 6.1, 7.4, 13.5, 17.4, 18.5, 20.7, 23.9, and 28.3.

79. On information and belief, following FDA approval of Apotex's ANDA, the Apotex ANDA Product will be used in a method of Philadelphia chromosome positive acute lymphoblastic leukemia in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a pharmaceutical composition. On further information and belief, the pharmaceutical composition of the Apotex ANDA Product comprises crystalline form of ponatinib hydrochloride according to claim 19 of the '895 patent.

80. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will infringe one or more claims of the '895 patent under 35 U.S.C. § 271(a) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States.

81. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will induce infringement of one or more claims of the '895 patent under 35 U.S.C. § 271(b) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, upon FDA approval of Apotex's ANDA, Apotex will intentionally encourage acts of direct infringement with knowledge of the '895 patent and knowledge that its acts are encouraging infringement.

82. Unless enjoined by this Court, upon FDA approval of Apotex's ANDA, Apotex will contributorily infringe one or more claims of the '895 patent under 35 U.S.C. § 271(c) by making, using, offering to sell, selling and/or importing the Apotex ANDA Product in the United States. On information and belief, Apotex has had and continues to have knowledge that the Apotex ANDA Product is especially adapted for a use that infringes one or more claims of the '895 patent and that there is no substantial non-infringing use for the Apotex ANDA Product.

83. Apotex has had knowledge of the claims of the '895 patent since at least the date Plaintiffs disclosed the asserted claims for the Patents-in-Suit including from the application that would issue as the '895 patent pursuant to Local Patent Rule 3.6(b) on November 19, 2021.

84. Plaintiffs will be substantially and irreparably harmed if Apotex is not enjoined from infringing the '895 patent. Plaintiffs do not have an adequate remedy at law.

85. This case is an exceptional one, and Plaintiffs are entitled to an award of its reasonable attorneys' fees under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request the following relief:

A. A Judgment that Apotex has infringed one or more claims of the '470 patent by submitting ANDA No. 215893;

B. A Judgment that Apotex has infringed, and that Apotex's making, using, selling, offering to sell, or importing the Apotex ANDA Product would constitute infringement of one or more claims of the '470 patent, and/or induce or contribute to infringement of one or more claims of the '470 patent pursuant to 35 U.S.C. § 271(a), (b) and/or (c);

C. A preliminary and permanent injunction restraining and enjoining Apotex, and its officers, agents, attorneys, and employees, and those acting in privity and/or concert with them, from engaging in the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of the Apotex ANDA Product until after the expiration of the '470 patent, or any later expiration of exclusivity to which Plaintiffs are or become entitled;

D. A permanent injunction, pursuant to 35 U.S.C. § 271(e)(4)(B), restraining and enjoining Apotex, its officers, agents, attorneys and employees, and those acting in privity and/or concert with them, from practicing any compounds, crystalline forms of ponatinib hydrochloride, compositions, or methods as claimed in the '470 patent, or from actively inducing or contributing to the infringement of any claim of the '470 patent, until after the expiration of the '470 patent, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

E. An Order that the effective date of any approval of ANDA No. 215893 relating to the Apotex ANDA Product be a date that is not earlier than the later of the expiration of the '470 patent, or any later expiration to which Plaintiffs are or become entitled;

F. To the extent that Apotex has committed any acts with respect to the compounds, crystalline forms of ponatinib hydrochloride, compositions, or methods claimed in the '470 patent, other than those acts expressly exempted by 35 U.S.C. § 271(e)(1), a Judgment awarding Plaintiffs damages for such acts;

G. If Apotex engages in the commercial manufacture, use, sale, offer for sale, and/or importation into the United States of the Apotex ANDA Products prior to the expiration of the '470 patent, a Judgment awarding damages to Plaintiffs resulting from such infringement, together with interest;

H. A Judgment declaring that the ’470 patent remain valid;

I. A Judgment that Apotex has infringed one or more claims of the ’897 patent by submitting ANDA No. 215893;

J. A Judgment that Apotex has infringed, and that Apotex’s making, using, selling, offering to sell, or importing the Apotex ANDA Product would constitute infringement of one or more claims of the ’897 patent, and/or induce or contribute to infringement of one or more claims of the ’897 patent pursuant to 35 U.S.C. § 271(a), (b) and/or (c);

K. A preliminary and permanent injunction restraining and enjoining Apotex, and its officers, agents, attorneys, and employees, and those acting in privity and/or concert with them, from engaging in the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of the Apotex ANDA Product until after the expiration of the ’897 patent, or any later expiration of exclusivity to which Plaintiffs are or become entitled;

L. A permanent injunction, pursuant to 35 U.S.C. § 271(e)(4)(B), restraining and enjoining Apotex, its officers, agents, attorneys and employees, and those acting in privity and/or concert with them, from practicing any crystalline forms of ponatinib hydrochloride, compositions, or methods as claimed in the ’897 patent, or from actively inducing or contributing to the infringement of any claim of the ’897 patent, until after the expiration of the ’897 patent, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

M. An Order that the effective date of any approval of ANDA No. 215893 relating to the Apotex ANDA Product be a date that is not earlier than the later of the expiration of the ’897 patent, or any later expiration to which Plaintiffs are or become entitled;

N. To the extent that Apotex has committed any acts with respect to the crystalline forms of ponatinib hydrochloride, compositions, or methods claimed in the '897 patent, other than those acts expressly exempted by 35 U.S.C. § 271(e)(1), a Judgment awarding Plaintiffs damages for such acts;

O. If Apotex engages in the commercial manufacture, use, sale, offer for sale, and/or importation into the United States of the Apotex ANDA Products prior to the expiration of the '897 patent, a Judgment awarding damages to Plaintiffs resulting from such infringement, together with interest;

P. A Judgment declaring that the '897 patent remain valid;

Q. A Judgment that Apotex has infringed one or more claims of the '895 patent by submitting ANDA No. 215893;

R. A Judgment that Apotex has infringed, and that Apotex's making, using, selling, offering to sell, or importing the Apotex ANDA Product would constitute infringement of one or more claims of the '895 patent, and/or induce or contribute to infringement of one or more claims of the '895 patent pursuant to 35 U.S.C. § 271(a), (b) and/or (c);

S. A preliminary and permanent injunction restraining and enjoining Apotex, and its officers, agents, attorneys, and employees, and those acting in privity and/or concert with them, from engaging in the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of the Apotex ANDA Product until after the expiration of the '895 patent, or any later expiration of exclusivity to which Plaintiffs are or become entitled;

T. A permanent injunction, pursuant to 35 U.S.C. § 271(e)(4)(B), restraining and enjoining Apotex, its officers, agents, attorneys and employees, and those acting in privity

and/or concert with them, from practicing methods as claimed in the '895 patent, or from actively inducing or contributing to the infringement of any claim of the '895 patent, until after the expiration of the '895 patent, or any later expiration of exclusivity to which Plaintiffs are or becomes entitled;

U. An Order that the effective date of any approval of ANDA No. 215893 relating to the Apotex ANDA Product be a date that is not earlier than the later of the expiration of the '895 patent, or any later expiration to which Plaintiffs are or become entitled;

V. To the extent that Apotex has committed any acts with respect to the methods claimed in the '895 patent, other than those acts expressly exempted by 35 U.S.C. § 271(e)(1), a Judgment awarding Plaintiffs damages for such acts;

W. If Apotex engages in the commercial manufacture, use, sale, offer for sale, and/or importation into the United States of the Apotex ANDA Products prior to the expiration of the '895 patent, a Judgment awarding damages to Plaintiffs resulting from such infringement, together with interest;

X. A Judgment declaring that the '895 patent remain valid;

Y. A Judgment that this is an exceptional case pursuant to 35 U.S.C. § 285 and awarding Plaintiffs its attorneys' fees incurred in this action;

Z. A Judgment awarding Plaintiffs its costs and expenses incurred in this action; and

AA. Such other and further relief as the Court may deem just and proper.

Dated: December 17, 2021

By: *s/Robert C. Brady*

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CERTIFICATION PURSUANT TO LOCAL CIVIL RULES 11.2 & 40.1

I hereby certify that, to the best of my knowledge, the matter in controversy is not the subject of any other action pending in any court or of any pending arbitration or administrative proceeding.

Dated: December 17, 2021

By: *s/Robert C. Brady*

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