IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ZOGENIX, INC. and ZOGENIX INTERNATIONAL LTD., Plaintiffs, v. APOTEX INC. and APOTEX Corp., Defendants.	C.A. No. _____

COMPLAINT

Zogenix, Inc. and Zogenix International Ltd. (collectively, "Plaintiffs" or "Zogenix") for their Complaint against Apotex Inc. and Apotex Corp. (collectively, "Defendants" or "Apotex") allege as follows:

NATURE OF ACTION

1. This is an action by Zogenix against Apotex for infringement of United States Patent Nos. 10,947,183 ("the '183 patent") and 10,950,331 ("the '331 patent") (collectively, "the Asserted Patents").

2. This action arises out of Apotex's filing of Abbreviated New Drug Application ("ANDA") No. 216108 seeking approval by the United States Food and Drug Administration ("FDA") to sell generic copies of Zogenix's Fintepla® (fenfluramine) oral solution, CIV (DEA Schedule IV controlled substance) product prior to the expiration of the Asserted Patents. Apotex's proposed generic fenfluramine hydrochloride oral solution, 2.2 mg base/mL product that is the subject of Apotex's ANDA No. 216108 is referred to herein as "Apotex's ANDA Product."

THE PARTIES

3. Plaintiff Zogenix, Inc. is a corporation organized and existing under the laws of Delaware and having a place of business at 5959 Horton Street, Emeryville, CA 94608. Zogenix, Inc. is a global biopharmaceutical company that develops and commercializes therapies for rare diseases. Zogenix, Inc. owns approved New Drug Application ("NDA") No. 212102 for 2.2 mg/mL fenfluramine for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older, which Zogenix sells under the registered name Fintepla®. Zogenix, Inc. has the sole right to market Fintepla® in the United States.

4. Plaintiff Zogenix International Ltd. is a corporation organized and existing under the laws of the England and Wales and having a place of business at The Pearce Building, West Street, Maidenhead, Berkshire SL6 1RL, UK. Zogenix International Ltd. is a wholly owned subsidiary of Zogenix, Inc.

5. Upon information and belief, Apotex Inc. is a Canadian corporation with its principal place of business at 150 Signet Drive, Toronto, Ontario M9L 1T9, Canada.

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

7. Upon information and belief, Apotex Corp. is a subsidiary of Apotex Inc.

8. Upon information and belief, Apotex Corp. is the designated U.S. agent for Apotex Inc. in accordance with 21 C.F.R. § 314.50(a) in connection with Apotex's ANDA No. 216108.

9. Upon information and belief, Apotex Corp. is a generic pharmaceutical company that distributes and sells generic pharmaceutical products in the State of Delaware and throughout the United States that are manufactured by Apotex Inc.

JURISDICTION AND VENUE

10. This action arises under the patent laws of the United States, Title 35, United States Code.

11. The Court has subject matter jurisdiction over this action pursuant to the provisions of 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

12. This Court has personal jurisdiction over Apotex Corp. because Apotex Corp. is incorporated in the State of Delaware.

13. Upon information and belief, Apotex's registered agent for service of process is Corporate Creations Network Inc., with an address at 3411 Silverside Road #104, Tatnall Building, Wilmington, Delaware 19810.

14. This Court has personal jurisdiction over Apotex Inc. under Fed. R. Civ. P. 4(k) because, upon information and belief, Apotex Inc. is organized under the laws of Canada.

15. This Court has personal jurisdiction over Apotex Inc. because at least one of the provisions under Del. Code Ann. Tit. 10, § 3104, is satisfied.

16. Upon information and belief, Apotex satisfies at least § 3104(c)(1) ("[t]ransacts any business or performs any character of work or service in the State"), § 3104(c)(2) ("[c]ontracts to supply services or things in this State"), § 3104(c)(3) ("[c]auses tortious injury in the State by an act or omission in this State"), and § 3104(c)(4) ("[c]auses tortious injury in the State or outside of the State by an act or omission outside the State if the person regularly does or

solicits business, engages in any other persistent course of conduct in the State or derives substantial revenue from services, or things used or consumed in the State").

17. This court also has personal jurisdiction over Apotex Inc. because this suit arises out of and relates to Apotex Inc.'s activities, in concert with Apotex Corp., that are, and will be, directed to Delaware.

18. Upon information and belief, following any FDA approval of Apotex's ANDA, Apotex Inc., in concert with Apotex Corp., will market and sell Apotex's ANDA Product that is the subject of the infringement claims in this action in the State of Delaware and throughout the United States, including in this Judicial District.

19. Upon information and belief, Apotex Inc., directly and through its subsidiaries, affiliates, or agents, including Apotex Corp., is in the business of manufacturing generic pharmaceuticals that it distributes or has distributed in the State of Delaware and throughout the United States.

20. Upon information and belief, Defendants are agents of each other and/or work in concert with each other on the development, obtaining of regulatory approval, manufacture, marketing, sale, and/or distribution of generic drugs, including the ANDA Product.

21. Upon information and belief, and as indicated by Apotex's Notice of Certification Under 21 U.S.C. § 355(j)(2)(B) (§ 505(j)(2)(B) of the Federal Food, Drug and Cosmetic Act) and 21 C.F.R. § 314.95 (the "Apotex Notice Letter") dated October 12, 2021, Apotex prepared and filed ANDA No. 216108 with the intention of seeking to market Apotex's ANDA Product nationwide, including within this Judicial District.

22. Apotex's infringing activities with respect to its filing of ANDA No. 216108 and its intent to commercialize and sell Apotex's ANDA Product have led and/or will lead to foreseeable harm and injury to Zogenix.

23. Venue is proper in this Judicial District under 28 U.S.C. § 1400(b) with regard to Apotex Corp., because, upon information and belief, Apotex Corp. resides in the State of Delaware and therefore Apotex's ANDA submission is sufficiently related to this District.

24. Venue is proper in this Judicial District under 28 U.S.C. § 1391 and § 1400(b) with regard to Apotex Inc., because, upon information and belief, Apotex Inc. is incorporated in Canada and may be sued in any judicial district in the United States in which Apotex Inc. is subject to the Court's personal jurisdiction.

BACKGROUND

Fintepla®

25. The active ingredient in Zogenix's Fintepla® product is fenfluramine hydrochloride.

26. Zogenix markets Fintepla® oral solution that contains 2.2 mg base/mL fenfluramine, equivalent to 2.5 mg/mL of the hydrochloride salt.

27. The FDA-approved Prescribing Information for Fintepla® states that fenfluramine hydrochloride is designated chemically as N-ethyl-α-methyl-3-(trifluoromethyl)phenethylamine hydrochloride.

28. Fenfluramine hydrochloride comprises two stereoisomers in a "racemic mixture" (1:1 mixture), which are referred to as "dexfenfluramine" and "levofenfluramine."

29. The precise mechanisms by which fenfluramine exerts its therapeutic effects in the treatment of seizures associated with Dravet syndrome are unknown.

30. Fenfluramine is an amphetamine analogue that increases the extracellular levels of 5-hydroxytryptamine (5-HT, serotonin) in nervous tissue.

31. It is currently theorized that fenfluramine acts by increasing extracellular levels of serotonin through interaction with serotonin transporter proteins, by exhibiting agonist activity at serotonin 5-HT1D, 5-HT-2A and 5-HT2C receptors, and by positively modulating the sigma-1 receptor.

32. Racemic fenfluramine was originally approved in the U.S. in 1973 as Pondimin® (20 mg and 60 mg tablets fenfluramine hydrochloride) and Ponderex® (20 mg capsules fenfluramine hydrochloride) for use as an anorectic agent and was prescribed both alone and in combination with phentermine ("fen-phen") as an appetite suppressant for the treatment of adult obesity. Dexfenfluramine was approved in the U.S. in 1996 as Redux® (15 mg capsules dexfenfluramine hydrochloride) also as an anorectic agent and was also prescribed both alone and in combination with phentermine ("dexfen-phen").

33. Fenfluramine was withdrawn from the worldwide market in the late 1990's (1997 in the U.S.) due to drug-related left-sided cardiac valvular disease.

34. On March 8, 1999, fenfluramine and the single stereoisomer dexfenfluramine were included in a Federal Register notice identifying drug products that were withdrawn from the U.S. market due to reasons of safety or effectiveness. (64 F.R. 10944.)

35. On September 29, 2015, the FDA provided notice in the Federal Register of its determination that Pondimin® (fenfluramine hydrochloride tablets, 20 mg and 60 mg) and Ponderex® (fenfluramine hydrochloride capsules, 20 mg) were withdrawn from the U.S. market due to reasons of safety or effectiveness. (80 F.R. 58490.)

36. On June 25, 2020, the FDA approved Zogenix's Fintepla® product for the treatment of seizures associated with Dravet syndrome in patients aged 2 and older.

37. Dravet syndrome is a life-threatening, rare and chronic form of childhood-onset epilepsy, often characterized by severe and unrelenting seizures despite medical treatment.

38. Dravet syndrome is difficult to treat with one or even two drugs, and generally requires three or four drugs to manage its severe and unrelenting seizures.

39. Zogenix demonstrated the effectiveness of Fintepla® for the treatment of seizures associated with Dravet syndrome in combination with other anti-epileptic drugs through two clinical studies.

40. The studies measured the change from baseline in the frequency of convulsive seizures.

41. In these studies, subjects treated with Fintepla® in combination with stiripentol, clobazam, and valproate had highly significant greater reductions in the frequency of convulsive seizures during the trials than subjects who received placebo, stiripentol, clobazam, and valproate. *See*, *e.g.*, Nabbout, R., Mistry, A., Zuberi, S., Villeneuve, N., Gil-Nagel, A., Sanchez-Carpintero, R., *et al*. (2020); Fenfluramine for treatment-resistant seizures in patients with Dravet syndrome receiving stiripentol-inclusive regimens: a randomized clinical trial. *JAMA Neurology*, 77(3), 300-308. These reductions were seen within 3-4 weeks and remained generally consistent over the 14- to 15-week treatment periods, and these reductions were similarly observed in long-term, open-label studies.

42. Zogenix also developed methods to treat, track, and protect Dravet patients taking fenfluramine products.

43. The methods Zogenix developed became part of a Risk, Evaluation, and Mitigation Strategy ("REMS") that is required by the FDA, in order to protect patients from heart-valve abnormalities.

44. The FDA requires a REMS for any sales of fenfluramine products, including fenfluramine hydrochloride drug products.

Orange Book Listing for Fintepla®

45. Zogenix, Inc. holds approved NDA No. 212102 for 2.2 mg/mL fenfluramine for the treatment of seizures associated with Dravet syndrome in patients 2 years of age and older, which Zogenix sells under the registered name Fintepla®.

46. Fintepla® has Orphan Drug Exclusivity that does not expire until June 25, 2027.

47. Because of Fintepla®'s Orphan Drug Exclusivity, no generic version of Fintepla® can be marketed until after June 25, 2027.

48. Pursuant to 21 U.S.C. § 355(b)(1) and the regulations the FDA has promulgated pursuant thereto, the Asserted Patents are among eleven patents listed in the FDA publication titled "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book") for the Fintepla® NDA, which appear in the Orange Book as follows:

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	9549909	05/03/2033			U-2858		07/24/2020
001	9603814	05/03/2033			U-2858		07/24/2020
001	9603815	05/03/2033			U-2858		07/24/2020
001	9610260	05/03/2033			U-2858		07/24/2020
001	10452815	06/29/2038			U-2859		07/24/2020

Product No	Patent No	Patent Expiration	Drug Substance	Drug Product	Patent Use Code	Delist Requested	Submission Date
001	10478441	05/03/2033			U-2860		07/24/2020
001	10478442	05/03/2033			U-2860		07/24/2020
001	10603290	08/02/2037			U-2861		07/24/2020
001	10947183	12/20/2036	DS	DP			04/06/2021
001	10950331	09/28/2035			U-3098		04/06/2021
001	11040018	08/02/2037			U-2861		07/22/2021

The ’183 Patent

49. On March 16, 2021, the USPTO issued the ’183 patent, titled “Fenfluramine Compositions and Methods of Preparing the Same.” The ’183 patent is duly and legally assigned to Zogenix International Ltd. A copy of the ’183 patent is attached hereto as Exhibit 1.

50. The claims of the ’183 patent are directed, *inter alia*, to improved forms of the fenfluramine active ingredient.

51. The expiration date for the ’183 patent is December 20, 2036.

The ’331 Patent

52. On March 16, 2021, the USPTO issued the ’331 patent, titled "Control System for Control of Distribution of Medication." The ’331 patent is duly and legally assigned to Zogenix International Ltd. A copy of the ’331 patent is attached hereto as Exhibit 2.

53. The claims of the ’331 patent are directed, *inter alia*, to treatment of refractory epilepsy patients with fenfluramine that reduces the risk of cardiovascular toxicity by using cardiac monitoring and restricted distribution.

54. The expiration date for the ’331 patent is September 28, 2035.

Apotex's ANDA No. 216108

55. By letter dated October 12, 2021 (the "Apotex Notice Letter"), and received by Zogenix by October 13, 2021, Apotex notified Zogenix that it had filed ANDA No. 216108 with the FDA, seeking approval under the Federal Food, Drug and Cosmetic Act to market and sell Apotex's ANDA Product – generic copies of Zogenix's Fintepla® product – prior to the expiration of the Asserted Patents.

56. The Apotex Notice Letter states that ANDA No. 216108 seeks to "obtain approval to engage in the commercial manufacture, use, or sale" of Apotex's ANDA Product prior to the expiration of the '183 patent and '331 patent.

57. The Apotex Notice Letter asserts that ANDA No. 216108 contains a "Paragraph IV" certification under 21 U.S.C. § 355(j)(2)(B)(iv)(II) alleging that the '183 patent and the '331 patent "are invalid, unenforceable and/or will not be infringed by the commercial manufacture, use, or sale" of Apotex's ANDA Product.

58. Attached to the Apotex Notice Letter was Apotex's Detailed Statement for ANDA No. 216108 ("Apotex's Detailed Statement") asserting the purported factual and legal bases for Apotex's contention that the '183 patent and '331 patent were invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, or sale of the drug product described in Apotex's ANDA.

59. Apotex's Detailed Statement alleges that all claims of the '183 patent and '331 patent were invalid.

60. Apotex's Detailed Statement does not contain a non-infringement argument with respect to claims 25-27 of the '183 patent.

61. Apotex's Detailed Statement does not contain a non-infringement argument with respect to all of the claims of the '331 patent.

62. Upon information and belief, upon approval of ANDA No. 216108, Apotex will sell and distribute Apotex's ANDA Product throughout the United States.

63. Upon information and belief, Apotex will sell and distribute Apotex's ANDA Product with a product label and REMS substantially the same as for the FDA-approved Fintepla® product.

64. The Asserted Patents listed in the Orange Book cover the use of Fintepla® as indicated on the FDA-approved Fintepla® product label and REMS, and are listed in the Orange Book for that reason.

65. Since Apotex's ANDA Product will have substantially the same label and REMS as the FDA-approved Fintepla® label, the sale and use of Apotex's ANDA Product with its label infringes the Asserted Patents, as detailed further below.

COUNT I

(Infringement of U.S. Patent No. 10,947,183)

66. The allegations of paragraphs 1-65 above are repeated and re-alleged as if set forth fully herein.

67. Pursuant to 35 U.S.C. § 271(e)(2)(A), Apotex's filing of ANDA No. 216108 seeking approval to market Apotex's ANDA Product is an act of infringement of at least claim 25 of the '183 patent entitling Zogenix to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an order of this Court that the effective date of approval for ANDA No. 216108 be a date which is not earlier than the expiration date of the '183 patent.

68. Claim 25 of the '183 patent recites:

> 25. A composition, comprising fenfluramine and at least one trifluoromethyl-phenyl regioisomer of fenfluramine, wherein the at least one trifluoromethyl-phenyl regioisomer of fenfluramine is present in some amount that is less than 0.2% by weight in total of trifluoromethyl-phenyl regioisomers of fenfluramine.

69. Apotex, in its Detailed Statement requiring that it disclose its non-infringement arguments for claim 25, did not disclose any arguments that its ANDA Product would not infringe claims 25, 26, and 27.

70. Under 35 U.S.C. § 271(e)(2)(A), "[i]t shall be an act of infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [i.e., an ANDA] . . . for a drug claimed in a patent . . . ."

71. Upon information and belief, Apotex has submitted Apotex's ANDA to market a generic version of Fintepla® that contains a fenfluramine active ingredient that infringes the '183 patent.

72. If Apotex's ANDA Product is approved, Apotex will make, use, import, or offer to sell or sell its ANDA Product in or into the United States, and these acts will infringe at least one claim of the '183 patent under 35 U.S.C. § 271(a), (b), (c), or (g).

73. Thus, Apotex's ANDA Product infringes the '183 patent under 35 U.S.C. § 271(e)(2)(A).

74. The foregoing actions by Apotex constitute infringement of at least claim 25 of the '183 patent.

75. Zogenix will be substantially and irreparably harmed if Apotex is not enjoined from infringing one or more claims of the '183 patent. Zogenix has no adequate remedy at law.

COUNT II

(Infringement of U.S. Patent No. 10,950,331)

76. The allegations of paragraphs 1-75 above are repeated and re-alleged as if set forth fully herein.

77. Pursuant to 35 U.S.C. § 271(e)(2)(A), Apotex's filing of ANDA No. 216108 seeking approval to market Apotex's ANDA Product is an act of infringement of at least claim 1 of the '331 patent entitling Zogenix to the relief provided by 35 U.S.C. § 271(e)(4), including, *inter alia*, an order of this Court that the effective date of approval for ANDA No. 216108 be a date which is not earlier than the expiration date of the '331 patent.

78. Claim 1 of the '331 patent recites:

> 1. A method of treating one or more refractory epilepsy patients with fenfluramine comprising:
>
> providing a data storage facility comprising a database of patient records, each patient record having a medication authorization field for entering a first prescription for fenfluramine to treat the patient;
>
> a central controller having one or more processors coupled to a communication network, which central controller is coupled to the data storage facility to read and write data to the data storage facility via the network; and
>
> wherein the central controller controls transmission and receipt of data to and from the data storage facility via the network,
>
> the central controller being programed to output via the network a first authorization of a first prescription of epilepsy medication to a patient previously subjected to one or more initial medical tests, each providing an initial medical test result,
>
> wherein the initial medical test is selected from the group consisting of a medical examination by a physician, a genetic test, a physiological function test, and a medical imaging test,

wherein output of the first authorization is dependent upon satisfactory results of one or more of the initial medical tests entered into each patient's record, and

further programed to schedule one or more subsequent tests for each patient prior to allowing entry of a prescription for epilepsy medication in the medication authorization field,

wherein at least one of said subsequent medical tests is an echocardiographic imaging test which echocardiographic imaging test is performed in a manner which provides measurements of dimensions of one or more internal heart structures and heart flow-rate, and the patient receives or continues to receive medication only on entry of satisfactory echocardiography assessment results,

wherein the central controller inhibits the authorization output of the first or subsequent prescriptions upon the entry of unsatisfactory test results;

wherein the central controller manages one or more aspects of the authorized prescription for the patient selected from the group consisting of dosage amount; volume dispensed; dosing regimen; and intended time period of use, whereby overuse or misuse of fenfluramine is inhibited and

wherein aggregated and analyzed data is reported to a regulatory agency.

79. Apotex, in its Detailed Statement requiring that it disclose its non-infringement arguments for claim 1 and the other asserted claims, did not provide arguments that its ANDA Product would not infringe all of the ’331 patent’s claims, but only alleged generally regarding “claims of the ’331 Patent” without specifying whether all, rather than just some, claims were alleged not to be infringed.

80. Under 35 U.S.C. § 271(e)(2)(A), “[i]t shall be an act of infringement to submit . . . an application under section 505(j) of the Federal Food, Drug, and Cosmetic Act [i.e., an ANDA] . . . for a drug claimed in a patent or the use of which is claimed in a patent . . . .”

81. Upon information and belief, Apotex has submitted Apotex's ANDA to market a generic Fintepla® for a method of treatment that infringes the '331 patent.

82. Upon information and belief, Apotex had knowledge of the '331 patent prior to infringement.

83. Upon information and belief, Apotex knew that the '331 patent was listed in the Orange Book prior to the filing of its ANDA.

84. Because the '331 patent covers the use of Fintepla®, as stated in the Orange Book, upon information and belief, Apotex knew that its filing of an ANDA to make a generic copy of Fintepla® would infringe the '331 patent.

85. Because the Fintepla® label and REMS encourages infringement of claim 1, and because, upon information and belief, Apotex's label and REMS will be substantially similar to Fintepla®'s label and REMS, Apotex will have a specific intent to actively encourage infringement of claim 1 by marketing its generic copy of Fintepla®.

86. Upon information and belief, Apotex will induce others to infringe and/or contribute to the infringement of at least claim 1 of the '331 patent under 35 U.S.C. § 271(b) and/or (c) by, among other things, actively and knowingly aiding and abetting others to infringe, including, but not limited to, the prescribers, purchasers, distributors, pharmacists, or users thereof.

87. Upon information and belief, if Apotex's ANDA Product is approved, Apotex will make, use, import, offer to sell or sell its ANDA Product in or into the United States, and thereby infringe directly or contribute to or induce infringement of at least one claim of the '331 patent, including at least claim 1, under 35 U.S.C. § 271(a), (b), (c), or (g).

88. Thus, Apotex's ANDA Product infringes the ’331 patent under 35 U.S.C. § 271(e)(2)(A).

89. The foregoing actions by Apotex constitute and/or would constitute infringement of at least claim 1 of the ’331 patent.

90. Zogenix will be substantially and irreparably harmed if Apotex is not enjoined from infringing or actively inducing or contributing to infringement of one or more claims of the ’331 patent. Zogenix has no adequate remedy at law.

PRAYER FOR RELIEF

WHEREFORE, Zogenix requests the following relief:

A. A judgment that Apotex’s submission of ANDA No. 216108 was an act of infringement and that Apotex’s making, using, selling, offering for sale, marketing, distributing, or importing Apotex’s ANDA Product prior to the expiration of the ’183 patent or ’331 patent will infringe each of those patents;

B. A judgment that the effective date of any FDA approval for Apotex to make, use, offer for sale, sell, market, distribute, or import Apotex’s ANDA Product shall be no earlier than the last date on which the ’183 patent and ’331 patent expire, or the later expiration of any exclusivity to which Zogenix is or becomes entitled;

C. A permanent injunction enjoining Apotex, its officers, agents, servants, and employees, and those persons in active concert or participation with any of them, from making, using, selling, offering for sale, marketing, distributing, or importing Apotex’s ANDA Product, and from inducing or contributing to any of the foregoing, prior to the expiration of the ’183 patent or ’331 patent, or the later expiration of any exclusivity to which Zogenix is or becomes entitled;

D. A judgment that this case is an exceptional case under 35 U.S.C. § 285, entitling Zogenix to an award of their reasonable attorneys' fees for bringing and prosecuting this action;

E. An award of Zogenix's costs and expenses in this action; and

F. Such further and additional relief as this Court deems just and proper.

Dated: October 28, 2021

BARNARD, MEZZANOTTE, PINNIE, SEELAUS & KRAFT, LLP

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