IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTELLAS PHARMA INC., ASTELLAS IRELAND CO., LTD. and ASTELLAS PHARMA GLOBAL DEVELOPMENT, INC.,	)	C.A. No. _____
Plaintiffs,	)	
v.	)	
APOTEX INC. and APOTEX CORP.	)	
Defendant.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs Astellas Pharma Inc., Astellas Ireland Co., Ltd. and Astellas Pharma Global Development, Inc. (collectively, "Astellas" or "Plaintiffs"), by their undersigned attorneys, hereby allege as follows:

NATURE OF ACTION

1. This is an action for patent infringement of United States Patent No. 10,842,780 ("the '780 Patent"), arising under the United States patent laws, Title 35, United States Code. This action relates to the Abbreviated New Drug Application ("ANDA") submitted by the above-named Defendants under Section 505(j) of the Federal Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(j), seeking United States Food and Drug Administration ("FDA") approval to market a generic pharmaceutical product.

THE PARTIES

A. Astellas Pharma Inc., Astellas Ireland Co., Ltd. and Astellas Pharma Global Development, Inc.

2. Plaintiff Astellas Pharma Inc. ("API") is a corporation organized and existing under the laws of Japan, having its principal place of business at 2-5-1, Nihonbashi-Honcho, Chuo-Ku, Tokyo 103-8411, Japan. API was formed on April 1, 2005, from the merger of Yamanouchi Pharmaceutical Co., Ltd. and Fujisawa Pharmaceutical Co., Ltd.

3. Plaintiff Astellas Ireland Co., Ltd. ("AICL") is a corporation organized and existing under the laws of Ireland, having its principal place of business at Damastown Road, Damastown Industrial Park, Mulhuddart, Dublin 15, Ireland. AICL is a subsidiary of Plaintiff API.

4. Plaintiff Astellas Pharma Global Development, Inc. ("APGD") is a corporation organized and existing under the laws of the State of Delaware, having its principal place of business at 1 Astellas Way, Northbrook, Illinois 60062. APGD is a subsidiary of Plaintiff API.

B. Apotex Inc. and Apotex Corp. (collectively, "Apotex")

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 M9L 1T9, Canada. On information and belief, Apotex Inc. is in the business of, *inter alia*, developing, manufacturing and/or distributing generic drug products for marketing, sale, and/or use throughout the United States including in this judicial district.

6. On information and belief, Defendant Apotex Corp. is a corporation organized and existing under the laws of Delaware, having a principal place of business at 2400 N. Commerce Parkway, Suite 400, Weston, Florida 33326. On information and belief, Apotex Corp. is in the business of, *inter alia*, developing, manufacturing and/or distributing generic drug products for marketing, sale, and/or use throughout the United States including in this judicial district.

7. By a letter dated June 22, 2021, ("Apotex's Notice Letter") Apotex notified Plaintiffs that Apotex had submitted to FDA ANDA No. 209434 for mirabegron extended-release tablets, 25 mg and 50 mg ("Apotex ANDA"), a drug product that is a generic version of Myrbetriq® extended-release tablets, in the 25mg and 50mg strengths ("Apotex's ANDA Product"). On information and belief, the purpose of Apotex's submission of the Apotex ANDA was to obtain approval under the FDCA to engage in the commercial manufacture, use, offer for sale, and/or sale of Apotex's ANDA Product prior to the expiration of the '780 Patent.

8. In Apotex's Notice Letter, Apotex notified Plaintiffs that, as a part of the Apotex ANDA, Apotex had filed a certification of the type described in Section 505(j)(2)(A)(vii)(IV) of the FDCA, 21 U.S.C. § 355(j)(2)(A)(vii)(IV), with respect to the '780 Patent, asserting it is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, and sale of Apotex's ANDA Product.

JURISDICTION AND VENUE

9. This Court has jurisdiction over the subject matter of this action under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202.

10. This Court has personal jurisdiction over Apotex because, among other things, Apotex has committed, or aided, abetted, contributed to, or participated in the commission of, tortious acts of patent infringement in filing the Apotex ANDA that has led to foreseeable harm and injury to Plaintiffs, and will imminently commit, or aid, abet, contribute to, or participate in the commission of, a tortious act of patent infringement by selling Apotex's ANDA Product which will lead to foreseeable harm and injury to Plaintiffs.

11. This Court also has personal jurisdiction over Apotex because its affiliations with the State of Delaware, including by virtue of Apotex Corp.'s incorporation in Delaware, are so continuous and systematic as to render Apotex essentially at home in this forum.

12. This Court also has personal jurisdiction over Apotex Inc. pursuant to Fed. R. Civ. P. 4(k)(2) because (a) Astellas's claims arise under federal law; (b) as a foreign defendant, Apotex Inc. is not subject to jurisdiction in any state's courts of general jurisdiction; and (c) Apotex Inc. has sufficient contacts within the United States as a whole, including but not limited to preparing and submitting an ANDA to FDA and/or manufacturing and/or selling pharmaceutical products distributed throughout the United States, such that this Court's exercise of jurisdiction over Apotex Inc. satisfies due process.

13. This Court also has personal jurisdiction over Apotex because it has frequently availed itself of the legal protections of the State of Delaware by, among other things, Apotex Corp. selecting the State of Delaware as its place of incorporation, and by Apotex admitting jurisdiction and asserting counterclaims in lawsuits filed in the United States District Court for the District of Delaware. *See, e.g., Bial Portela & CA SA et al. v. Apotex Inc. et al.*, C.A. No. 21-00187 (D. Del.), D.I. 6; *Intercept Pharm., Inc. et al. v. Apotex Inc. et al.*, C.A. No. 20-1105 (D. Del.), D.I. 10.

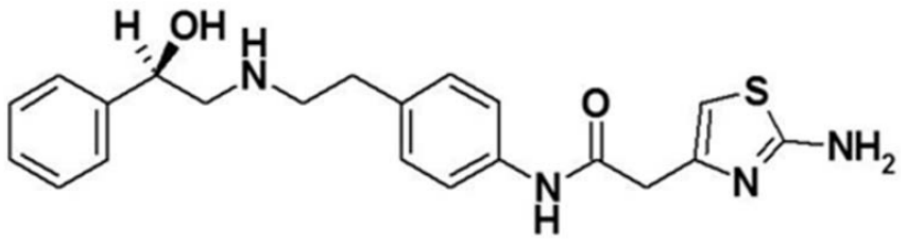
14. For these reasons, and for other reasons that will be presented to the Court if jurisdiction is challenged, the Court has personal jurisdiction over Apotex.

15. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391 and 1400(b) and/or Fed. R. Civ. P. 4(k)(2).

MYRBETRIQ® TABLETS

16. APGD holds approved New Drug Application ("NDA") No. 202611 for Myrbetriq® extended-release tablets, 25 mg and 50 mg, which contain the active ingredient, mirabegron. FDA approved NDA No. 202611 on June 28, 2012 for both the 25 mg and 50 mg extended-release Myrbetriq® tablets.

17. Mirabegron has been referred to chemically as, *inter alia*, (R)-2-(2-aminothiazol-4-yl)-4'-[2-(2-hydroxy-2-phenylethyl)amino]ethyl]acetic acid anilide, (R)-2-(2-aminothiazol-4-yl)-4'-[2-[(2-hydroxy-2-phenylethyl)amino]ethyl]acetanilide, and 2-(2-aminothiazol-4-yl)-N-[4-(2-{[(2R)-2-hydroxy-2-phenylethyl]amino}ethyl)phenyl]acetamide. Mirabegron can be depicted as, *inter alia*, the following formula:



18. Myrbetriq® extended-release tablets, containing 25 mg or 50 mg of mirabegron ("Myrbetriq® Tablets"), are indicated for the treatment of overactive bladder ("OAB") with symptoms of urge urinary incontinence, urgency, and urinary frequency.

19. Myrbetriq® Tablets comprise a sustained release hydrogel-forming formulation containing, *inter alia*, polyethylene oxide and polyethylene glycol as inactive ingredients within the tablet formulation, which function as a means for forming a hydrogel and a means for ensuring penetration of water into the tablets.

20. For quality control purposes in the U.S. market, Myrbetriq® Tablets are subjected to dissolution testing using the United States Pharmacopeia ("USP") Apparatus I. A dissolution test evaluates the rate and extent that a compound forms a solution under carefully controlled conditions. Within the context of regulatory approval, the USP dissolution test helps safeguard against the release of drug products that do not perform acceptably. USP Apparatus I (basket) and II (paddle) provide a platform to evaluate the *in vitro* performance of dosage forms using

standardized conditions. These two apparatus, and associated procedures, have become widely used and accepted.

21. When measured in accordance with the United States Pharmacopeia ("USP") dissolution apparatus II, using 900 mL of USP buffer and having a pH of 6.8 at a paddle rotation speed of 200 rpm ("USP II Method"), the Myrbetriq® Tablets release 39% or less of mirabegron after 1.5 hours, and at least 75% mirabegron after 7 hours.

THE PATENT-IN-SUIT

22. The United States Patent & Trademark Office ("PTO") duly and legally issued the '780 Patent, entitled "Pharmaceutical Composition for Modified Release," on November 24, 2020. A true and correct copy of the '780 Patent is attached as **Exhibit A**.

23. The '780 Patent is listed in FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") in connection with Myrbetriq® Tablets.

24. API is the record owner and assignee of the '780 Patent.

25. The '780 Patent will expire no earlier than September 28, 2029 and has pediatric exclusivity through March 28, 2030.

26. AICL is the exclusive licensee of the '780 Patent with the rights to develop, import, market, sell, distribute, and promote any and all pharmaceutical formulations in finished package forms which contain mirabegron as the active ingredient in the United States.

27. APGD has contracted with AICL to, *inter alia*, clinically develop mirabegron, prepare and submit NDA No. 202611 for marketing approval of Myrbetriq® Tablets in the United States.

28. AICL has contracted with Astellas Pharma US, Inc., a subsidiary of API to, *inter alia*, market and sell Myrbetriq® Tablets, in the United States on its behalf.

29. Myrbetriq® Tablets are covered by one or more claims of the '780 Patent.

MIRABEGRON ANDA FILERS

30. In June 2013, FDA issued a notice in the Federal Register (78 Fed. Reg. 37230 at 31 (June 20, 2013)) regarding bioequivalence guidance to be published on its website for mirabegron ANDAs. On its website, FDA lists the following dissolution requirements for mirabegron ANDA filers in order to establish bioequivalence with Myrbetriq® Tablets ("Mirabegron Bioequivalence Guidance"):

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (mL)	Recommended Sampling Times (minutes)	Date Updated
Mirabegron	Tablet (Extended Release)	I (Basket)	100	Phosphate Buffer, pH 6.8	900	1, 3, 5, 7, 8.5, 10 and 12 hours	05/09/2013

31. On information and belief, each mirabegron ANDA filer will be required to meet this dissolution method, or an equivalent dissolution method, to meet its bioequivalence requirements for its proposed ANDA product using Myrbetriq® Tablets as the reference standard. On information and belief, a proposed mirabegron ANDA product will have equivalent dissolution properties to Myrbetriq® Tablets as measured by USP Apparatus I and II.

CLAIMS FOR RELIEF

COUNT I: INFRINGEMENT OF THE '780 PATENT BY APOTEX

32. Plaintiffs incorporate by reference and reallege paragraphs 1 through 31 above as though fully restated herein.

33. Apotex, by filing ANDA No. 209434, has necessarily represented to FDA that, upon approval, Apotex's ANDA Product will have the same active ingredient, method of administration, dosage form, and dosage amount as Myrbetriq® Tablets, and will be bioequivalent to Myrbetriq® Tablets.

34. Apotex has indicated, including *inter alia* via Apotex's Notice Letter, its intent to engage in the commercial manufacture, use, offer for sale, sale, marketing, distributing, and/or importation of Apotex's ANDA Product prior to the expiration of the '780 Patent's patent term and pediatric exclusivity period.

35. On information and belief, and as required by the Mirabegron Bioequivalence Guidance, Apotex uses the dissolution method (or its equivalent) to establish Apotex's ANDA Product is bioequivalent to Myrbetriq® Tablets. On information and belief, Apotex's ANDA Product will have equivalent dissolution properties, as measured by USP Apparatus I and II, to Myrbetriq® Tablets, which uses a hydrogel formulation. On information and belief, because of the dissolution requirements contained within the Mirabegron Bioequivalence Guidance, including the use of Myrbetriq® Tablets as the reference standard, Apotex's ANDA Product uses a hydrogel formulation, the same as or equivalent to the Myrbetriq® Tablets formulation, that is covered by one or more claims of the '780 Patent.

36. On information and belief, Apotex relied on, *inter alia*, Apotex's dissolution data to conclude that Apotex's ANDA Product is bioequivalent to Astellas's Myrbetriq® Tablets.

37. In Apotex's Notice Letter, Apotex does not deny that Apotex's ANDA Product is covered by one or more claims of the '780 Patent.

38. Apotex's submission of ANDA No. 209434 seeking approval to engage in the commercial manufacture, use, offer to sell, or sale of Apotex's ANDA Product, prior to the expiration of the '780 Patent, constitutes infringement of one or more of the claims of the '780 Patent under 35 U.S.C. § 271(e)(2)(A).

39. Unless Apotex is enjoined by the Court, Plaintiffs will be substantially and irreparably harmed by Apotex's infringement of the '780 Patent. Plaintiffs do not have an adequate remedy at law.

40. Plaintiffs are commencing this action within 45 days of receiving Apotex's Notice Letter pursuant to 21 U.S.C. § 355(j)(5)(B)(iii).

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs API, AICL, and APGD, pray for a judgment in their favor and against Apotex, and respectfully request the following relief:

A. A judgment that Apotex's submission and maintenance of its ANDA (*i.e.*, the Apotex ANDA) constituted an act of infringement of the '780 Patent;

B. A judgment (or a declaration) that Apotex's making, using, offering to sell, or selling in the United States or importing into the United States of its Proposed ANDA Product (*i.e.*, Apotex's ANDA Product) will infringe the '780 Patent;

C. A permanent injunction restraining and enjoining Apotex, its affiliates, subsidiaries, officers, agents, attorneys and employees, and those acting in privity or concert with Apotex, from engaging in the commercial manufacture, use, offer for sale, or sale within the United States, or importation into the United States, of its Proposed ANDA Product until the expiration of the '780 Patent, including its pediatric exclusivity period and any other extensions and/or periods of exclusivity to which Plaintiffs and/or the '780 Patent are or become entitled;

D. An order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any approval of Apotex's ANDA shall be a date that is not earlier than the expiration date of the '780 Patent, including its pediatric exclusivity period and any other extensions and/or periods of exclusivity to which Plaintiffs and/or the '780 Patent are or become entitled;

E. Damages, including monetary and other relief, to Plaintiffs if Apotex engages in commercial manufacture, use, offers to sell, sale, or importation into the United States of its Proposed ANDA Product, prior to the expiration date of the '780 Patent, including its pediatric exclusivity period and any other extensions and/or additional periods of exclusivity to which Plaintiffs are or become entitled;

F. A declaration that this case is "exceptional" within the meaning of 35 U.S.C. § 285 and an award of reasonable attorney fees, costs, expenses, and disbursements of this action; and

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

Dated: August 5, 2021

MCCARTER & ENGLISH, LLP

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