IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTELLAS PHARMA INC., ASTELLAS IRELAND CO., LTD. and ASTELLAS PHARMA GLOBAL DEVELOPMENT, INC.,	)	Case No. _____
Plaintiffs,	)	
v.	)	
ASCENT PHARMACEUTICALS, INC.,	)	
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:

THE PARTIES

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

1. 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.

2. 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.

3. 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. Ascent Pharmaceuticals, Inc. ("Ascent" or "Defendant")

4. On information and belief, Ascent is a corporation organized and existing under the laws of the State of New York, having a principal place of business at 400 South Technology Drive, Central Islip, New York.

5. On information and belief, Ascent is in the business of, *inter alia*, developing, preparing, manufacturing, selling, marketing, and distributing generic pharmaceutical products throughout the United States, including in this judicial district.

6. By a letter dated March 22, 2023 ("Ascent's Notice Letter"), Ascent notified Plaintiffs that Ascent had submitted to the United States Food and Drug Administration ("FDA") Abbreviated New Drug Application ("ANDA") No. 218172 for mirabegron extended-release tablets, 25 mg and 50 mg ("Ascent ANDA"), a drug product that is a generic version of Myrbetriq® extended-release tablets, in the 25 and 50 mg strengths ("Ascent's ANDA Product"). On information and belief, the purpose of Ascent's submission of the Ascent ANDA was to obtain approval under the Federal Food, Drug, and Cosmetic Act ("FDCA") to engage in the commercial manufacture, use, offer for sale, and/or sale of Ascent's ANDA Product Prior to March 28, 2030.

7. In Ascent's Notice Letter, Ascent notified Plaintiffs that as part of the Ascent ANDA, Ascent 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) ("Paragraph IV certification"), with respect to one of the then-listed patents in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluation ("Orange Book"), asserting that it is invalid, unenforceable, and/or will not be infringed

by the commercial manufacture, use, and sale of Ascent's ANDA Product.

NATURE OF ACTION

8. 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 ANDA submitted by Ascent under Section 505(j) of the FDCA, 21 U.S.C. § 355(j), seeking FDA approval to market generic pharmaceutical products.

JURISDICTION AND VENUE

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

10. This Court has personal jurisdiction over Ascent because, *inter alia*, Ascent has committed, or aided, abetted, contributed to, or participated in the commission of, tortious acts of patent infringement in filing ANDA No. 218172 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 its ANDA Product throughout the United States and in this judicial district, which will lead to foreseeable harm and injury to Plaintiffs.

11. The Court also has personal jurisdiction over Ascent because, *inter alia*, this action arises from actions of Ascent directed toward Delaware, and because Ascent has purposefully availed itself of the rights and benefits of Delaware law by engaging in systematic and continuous contacts with Delaware. Upon information and belief, Ascent regularly and continuously transacts business within Delaware, including by selling pharmaceutical products in Delaware, either on its own or through its affiliates. Upon information and belief, Ascent derives substantial revenue from the sale of those products in Delaware and has availed itself of the privilege of conducting business in Delaware.

12. This Court also has personal jurisdiction over Ascent because it has frequently availed

itself of the legal protections of the State of Delaware, by, among other things, admitting jurisdiction and asserting counterclaims in lawsuits filed in the United States District Court for the District of Delaware. *See, e.g., Vifor Pharma, Inc. et al. v. Alkem Laboratories Ltd. et al.*, 20-106 (D. Del.); *Anacor Pharmaceuticals, Inc. v. Ascent Pharmaceuticals, Inc., et al.*, 18-1673 (D. Del.); *Purdue Pharma L.P., et al. v. Ascent Pharmaceuticals, Inc.*, C.A. No. 18-855 (D. Del.); *Purdue Pharma L.P., et al. v. Ascent Pharmaceuticals, Inc.*, C.A. No. 18-83 (D. Del.).

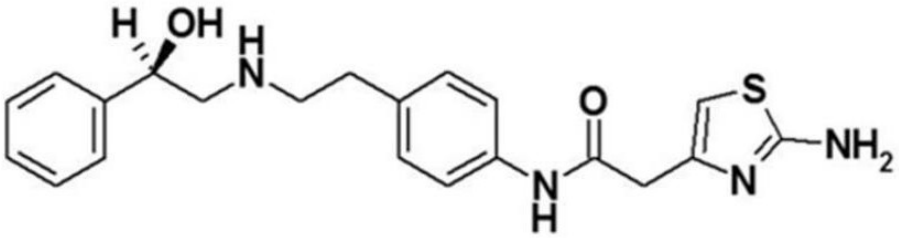
13. For these reasons, and for other reasons that will be presented to the Court if jurisdiction is challenged, the Court has personal jurisdiction over Ascent.

14. Venue is proper in this Court pursuant to 28 U.S.C. §§ 1391 and 1400(b).

MYRBETRIQ® TABLETS

15. 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. The FDA approved NDA No. 202611 on June 28, 2012 for both the 25 mg and 50 mg extended-release Myrbetriq® tablets.

16. 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:



17. 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.

18. Myrbetriq® Tablets comprise a sustained release hydrogel-forming formulation containing, *inter alia*, a means for forming a hydrogel and a means for ensuring penetration of water into the tablets.

19. 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.

20. 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.

21. The '780 Patent is listed in the Orange Book in connection with NDA 202611 as covering Myrbetriq®.

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. API is the record owner and assignee of the ’780 Patent.

24. The ’780 Patent will expire no earlier than September 28, 2029.

25. The ’780 Patent’s pediatric exclusivity extends to 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 DEFENDANT UNDER 35 U.S.C. § 271(e)(2)(A) AND 35 U.S.C. § 271(a)

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

33. Ascent, by filing ANDA No. 218172, has necessarily represented to the FDA that, upon approval, Ascent'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. Ascent, via its Notice Letter, has indicated its intent to engage in the commercial manufacture, use, offer for sale, sale, marketing, distributing, and/or importation of Ascent's ANDA Product prior to the expiration of the '780 Patent's patent term and pediatric exclusivity period.

35. Ascent's submission of ANDA No. 218172 seeking approval to engage in the commercial manufacture, use, offer to sell, or sale of Ascent'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).

36. On information and belief, Ascent intends to engage in the commercial manufacture, use, offer for sale, sale, marketing, distributing, and/or importation of Ascent's ANDA Product upon final approval of ANDA No. 218172 and prior to the expiration of the pediatric exclusivity associated with the '780 Patent.

37. Astellas has not received from Ascent notice of its filing of a Paragraph IV certification for its ANDA Product as to any other patent listed in the Orange Book for Myrbetriq® other than the '780 Patent. On information and belief, Ascent has filed certifications of the type described in Section 505(j)(2)(A)(vii)(III) of the FDCA, 21 U.S.C. § 355(j)(2)(A)(vii)(III) ("Paragraph III certification"), with respect to the other Orange Book listed patents for Myrbetriq®, including United States Patent Nos.: 7,342,117; 7,982,049; 8,835,474; and RE44,872.

38. Ascent's ANDA Product contains either 25 mg or 50 mg of mirabegron in extended-release tablets. Ascent's ANDA Product will also be bioequivalent to Myrbetriq® Tablets.

39. On information and belief, and as required by the Mirabegron Bioequivalence Guidance, Ascent uses the dissolution method (or its equivalent) to establish Ascent's ANDA Product is bioequivalent to Myrbetriq® Tablets. On information and belief, Ascent's ANDA Product will have equivalent dissolution properties, as measured by USP Apparatus I and II, to Myrbetriq® Tablets, which use 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, Ascent'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.

40. On information and belief, Ascent's ANDA Product contains a hydrogel-forming polymer and an additive that meet the claim limitations of one or more claims of the '780 Patent. Ascent's Notice Letter does not dispute that its ANDA Product contains such an additive nor one or more of the hydrogel-forming polymers listed in the claims of the '780 Patent.

41. On information and belief, and based on the representations in Ascent's Notice Letter, Ascent's ANDA Product is a sustained release hydrogel forming formulation of mirabegron having either 25 mg or 50 mg mirabegron, containing, *inter alia*, a hydrogel-forming polymer and an additive that are covered by one or more claims of the '780 Patent and having a dissolution profile meeting the dissolution rate element of the claims.

42. The commercial manufacture, use, offer for sale, sale, marketing, distributing, and/or importation of Ascent's ANDA Product would infringe one or more claims of the '780 Patent, or their equivalents, under 35 U.S.C. § 271(a).

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

COUNT II: CONTRIBUTORY INFRINGEMENT OF THE '780 PATENT BY DEFENDANT UNDER 35 U.S.C. § 271(c)

44. Plaintiffs incorporate by reference and reallege paragraphs 1 through 43 above as though fully restated herein.

45. On information and belief, if ANDA No. 218172 is approved by the FDA, Ascent will manufacture Ascent's ANDA Product, and will, without authority, induce or cause others to import Ascent's ANDA Product into the United States, or will offer to sell or sell Ascent's ANDA Product within the United States.

46. Ascent's ANDA Product constitutes a material part of the inventions covered by the claims of the '780 Patent and has no substantial non-infringing uses.

47. On information and belief, Ascent has had, and continues to have, knowledge that there is no substantial non-infringing use for Ascent's ANDA Product.

48. Ascent's actions will constitute contributory infringement of the '780 Patent

pursuant to 35 U.S.C. § 271(c).

49. As a result of the foregoing facts, there is a real, substantial, and continuing justiciable controversy between Plaintiffs and Ascent as to the liability of Ascent's infringement of the '780 Patent. Ascent's actions have created in Plaintiffs a reasonable apprehension of irreparable harm and loss resulting from Ascent's threatened imminent actions.

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

COUNT III: INDUCED INFRINGEMENT OF THE '780 PATENT BY DEFENDANT UNDER 35 U.S.C. § 271(b)

51. Plaintiffs incorporate by reference and reallege paragraphs 1 through 50 above as though fully restated herein.

52. On information and belief, if ANDA No. 218172 is approved by the FDA, Ascent will manufacture Ascent's ANDA Product, and will, without authority, induce or cause others to import Ascent's ANDA Product into the United States, offer for sale or sell Ascent's ANDA Product in the United States, or use Ascent's ANDA Product in the United States.

53. Ascent's ANDA Product and the use thereof would directly infringe the '780 Patent under 35 U.S.C. § 271(a).

54. On information and belief, Ascent has had, and continues to have, knowledge of the '780 Patent.

55. On information and belief, Ascent has had, and continues to have, knowledge that Ascent's ANDA Product and the use thereof would directly infringe the '780 Patent.

56. Ascent's inducement of others to import Ascent's ANDA Product into the United States, offer for sale or sell Ascent's ANDA Product in the United States, or use Ascent's ANDA

Product in the United States will aid and abet the direct infringement of the '780 Patent.

57. On information and belief, Ascent specifically intends to induce infringement of the '780 Patent.

58. Ascent's actions will constitute inducement of infringement of the '780 Patent pursuant to 35 U.S.C. § 271(b).

59. As a result of the foregoing facts, there is a real, substantial, and continuing justiciable controversy between Plaintiffs and Ascent as to the liability of Ascent's infringement of the '780 Patent. Ascent's actions have created in Plaintiffs a reasonable apprehension of irreparable harm and loss resulting from Ascent's threatened imminent actions.

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

PRAYER FOR RELIEF

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

A. A judgment that the Defendant's submission and maintenance of ANDA No. 218172 constituted an act of infringement of the '780 Patent;

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

C. A permanent injunction restraining and enjoining Ascent, its affiliates, subsidiaries, and each of its officers, agents, attorneys and employees, and those acting in privity or concert with it, from engaging in the commercial manufacture, use, offer for sale, or sale

within the United States, or importation into the United States, of Ascent's ANDA Product until the expiration of the '780 Patent, including any 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 Ascent's ANDA shall be a date that is not earlier than the expiration date of the '780 Patent, including any 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 Ascent engages in commercial manufacture, use, offers to sell, sale, or importation into the United States of Ascent's Proposed ANDA Product, prior to the expiration date of the '780 Patent, including any extensions and/or additional periods of exclusivity to which Plaintiffs and/or the '780 Patent 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: May 3, 2023

MCCARTER & ENGLISH, LLP

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