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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

OTSUKA PHARMACEUTICAL CO., LTD. Plaintiff, v. TORRENT PHARMACEUTICALS LIMITED, TORRENT PHARMA INC. and HETERO LABS LIMITED, Defendants.	Civil Action No.: 14-cv-4671-JBS-KMW

THIRD AMENDED COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Otsuka Pharmaceutical Co., Ltd. ("Otsuka"), by way of Complaint against defendants Torrent Pharmaceuticals Limited ("Torrent Ltd."), Torrent Pharma Inc. ("Torrent Inc.") and Hetero Labs Limited (collectively, "Defendants"), alleges as follows:

THE PARTIES

1. Otsuka is a corporation organized and existing under the laws of Japan with its corporate headquarters at 2-9 Kanda Tsukasa-machi, Chiyoda-ku, Tokyo, 101-8535, Japan.

Otsuka is engaged in the research, development, manufacture and sale of pharmaceutical products.

2. Upon information and belief, Torrent Ltd. is a corporation organized and existing under the laws of India, having its principal place of business at Torrent House, Off Ashram Road, Ahmedabad, 380009, Gujarat, India.

3. Upon information and belief, Torrent Inc. is a wholly-owned subsidiary of Torrent Ltd. Upon information and belief, Torrent Inc. is a corporation organized and existing under the laws of Delaware with its corporate headquarters at 150 Allen Road, Suite 102, Basking Ridge, New Jersey 07920.

4. Upon information and belief, Hetero Labs Limited is a corporation organized and existing under the laws of India, having its principal place of business at 7-2-A2, Hetero Corporate Industrial Estates, Sanath Nagar, Hyderabad – 500 018, Andhra Pradesh, India.

NATURE OF THE ACTION

5. This is an action for infringement of U.S. Patent No. 8,642,760 ("the '760 patent") and U.S. Patent No. 8,759,350 ("the '350 patent"), arising under the United States patent laws, Title 35, United States Code, § 100 *et seq*., including 35 U.S.C. §§ 271 and 281. This action relates to Torrent Ltd.'s filing of an Abbreviated New Drug Application ("ANDA") under Section 505(j) of the Federal Food, Drug and Cosmetic Act ("the Act"), 21 U.S.C. § 355(j), seeking U.S. Food and Drug Administration ("FDA") approval to manufacture, use, sell, offer to sell and import generic pharmaceutical products ("Torrent Ltd.'s generic products") prior to the expiration of the asserted patents, as well as Defendants' actual manufacture, market, import, use, sale and offer for sale of Torrent Ltd.'s generic products upon approval of its ANDA.

JURISDICTION AND VENUE

6. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338(a).

7. This Court has jurisdiction over Torrent Ltd. Torrent Ltd. is in the business of manufacturing, importing, marketing and selling pharmaceutical drug products, including generic drug products. Upon information and belief, Torrent Ltd., directly or through its wholly-owned subsidiaries (primarily Torrent Inc.), manufactures, imports, markets and sells generic drug products throughout the United States and in this judicial district. Upon information and belief, Torrent Ltd. purposefully has conducted and continues to conduct business directly, or through its wholly-owned subsidiaries (primarily Torrent Inc.), in this judicial district, and this judicial district is a likely destination of Torrent Ltd.'s generic products. Torrent Ltd. has previously submitted to the jurisdiction of this Court and has further previously availed itself of this Court by asserting counterclaims in other civil actions initiated in this jurisdiction.

8. Upon information and belief, this Court additionally has jurisdiction over Torrent Ltd. because it has availed itself of the rights and benefits of this judicial district, having stated in a purported Offer of Confidential Access, dated June 11, 2014, that "[t]he Company agrees that any claims for breach of this Agreement must be brought exclusively in the courts located in the State of New Jersey and consents to the jurisdiction and venue of such courts for any such claims."

9. This Court has jurisdiction over Torrent Inc. Upon information and belief, Torrent Inc.'s corporate headquarters are in New Jersey. Torrent Inc., directly or indirectly, manufactures, imports, markets and sells generic drugs throughout the United States and in this judicial district. Torrent Inc. has previously submitted to the jurisdiction of this Court and has

further previously availed itself of this Court by asserting counterclaims in other civil actions initiated in this jurisdiction.

10. Upon information and belief, Torrent Ltd. and Torrent Inc. operate as a single, integrated business, and share a website, http://www.torrentpharma.com, in which Torrent Inc. is identified as "general inquiries contact" and "business development contact" regarding Torrent operations in the United States. The website, http://www.torrentpharma.com/int_usa.php#, also states that: "The world's largest market for pharmaceuticals, USA, has always been on Torrent Pharma's strategic radar. That intent has been converted in early 2004 into a concrete undertaking, a fully owned subsidiary called Torrent Pharma Inc. This was floated to serve a large and growing need for high quality yet affordable medicines in the USA."

11. This Court has jurisdiction over Hetero Labs Limited. According to its website, "Hetero is the leading global supplier of APIs . . . to the pharmaceutical companies who manufacture formulations and new-generation products." *See* http://www.heteroworld.com/pages/business-api/. Upon information and belief, Hetero Labs Limited, directly or indirectly, manufactures, imports, markets and sells generic drugs throughout the United States and in this judicial district. Upon information and belief, Hetero Labs Limited maintains continuous and systematic contacts with New Jersey through its authorized U.S. agent, PharmaQ, Inc., located at Water View Plaza, 20001 Route 46, Suite 405, Parsippany, NJ 07054-1315.

12. Venue is proper in this judicial district under 28 U.S.C. §§ 1391(b) and (c), and §l400(b).

FIRST COUNT FOR PATENT INFRINGEMENT

13. The U.S. Patent and Trademark Office ("PTO") issued the '760 patent on February 4, 2014, entitled "Low Hygroscopic Aripiprazole Drug Substance and Processes for the Preparation Thereof." A copy of the '760 patent is attached as Exhibit A.

14. Otsuka is the owner of the '760 patent by virtue of assignment.

15. The '760 patent expires on March 25, 2023 (including pediatric exclusivity).

16. The '760 patent is directed to and claims, *inter alia,* aripiprazole drug substance.

17. Otsuka is the holder of New Drug Application ("NDA") No. 21-436 for aripiprazole tablets, which the FDA approved on November 15, 2002.

18. Otsuka lists the '760 patent in Approved Drug Products with Therapeutic Equivalence Evaluations ("the Orange Book") for NDA No. 21-436.

19. Otsuka markets aripiprazole tablets in the United States under the trademark Abilify®.

20. Upon information and belief, Torrent Ltd. submitted ANDA No. 20-1519 to the FDA, under Section 505(j) of the Act, 21 U.S.C. § 355(j), seeking approval to manufacture, use, import, offer to sell and sell Torrent Ltd.'s generic products in the United States.

21. Otsuka received a letter from Torrent Ltd. dated June 11, 2014, purporting to include a Notice of Certification for ANDA No. 20-1519 under 21 U.S.C. § 355(j)(2)(B) and 21 C.F.R. § 314.95 ("Torrent Ltd.'s June 11, 2014 letter") as to the '760 patent.

22. Torrent Ltd.'s June 11, 2014 letter alleges that the "name for the drug product that is the subject of the Torrent ANDA is aripiprazole tablet, for oral administration."

23. Upon information and belief, Torrent Ltd.'s generic products will, if approved and marketed, infringe at least one claim of the '760 patent.

24. Upon information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed at least one claim of the '760 patent by submitting, or causing to be submitted to the FDA, ANDA No. 20-1519 seeking approval to manufacture, use, import, offer to sell and sell Torrent Ltd.'s generic products before the expiration date of the '760 patent.

25. Upon information and belief, Torrent Ltd.'s actions relating to Torrent Ltd.'s ANDA No. 20-1519 complained of herein were done with the cooperation, participation and assistance, and for the benefit, of Torrent Inc., Torrent Ltd. and Hetero Labs Limited.

SECOND COUNT FOR PATENT INFRINGEMENT

26. Otsuka realleges, and incorporates in full herein, paragraphs 13-23 and 25.

27. Torrent Ltd.'s ANDA No. 20-1519 was approved by the FDA on April 28, 2015.

28. Upon information and belief, Defendants are currently manufacturing, marketing, importing, using, selling and offering for sale Torrent Ltd.'s generic products.

29. Upon information and belief, Defendants are infringing at least one claim of the '760 patent under 35 U.S.C. § 271(a) by their manufacture, market, import, use, sale and offer for sale of Torrent Ltd.'s generic products.

THIRD COUNT FOR PATENT INFRINGEMENT

30. Otsuka realleges, and incorporates in full herein, paragraphs 17-22.

31. The PTO issued the '350 patent on June 24, 2014, entitled "Carbostyril Derivatives and Serotonin Reuptake Inhibitors for Treatment of Mood Disorders." A copy of the '350 patent is attached as Exhibit B.

32. Otsuka is the owner of the '350 patent by virtue of assignment.

33. The '350 patent expires on March 2, 2027, subject to any supplemental patent term adjustment.

34. Otsuka lists the '350 patent in the Orange Book for NDA No. 21-436.

35. Defendants have actual knowledge of the '350 patent.

36. The '350 patent is directed to and claims, *inter alia,* novel pharmaceutical compositions comprising aripiprazole in combination with at least one of the antidepressant drugs citalopram or escitalopram, as well as methods of treating certain mood disorders comprising administering novel pharmaceutical compositions comprising aripiprazole in combination with at least one of citalopram or escitalopram.

37. Based on the knowledge of a person of ordinary skill in the art and the disclosures of the '350 patent and its prosecution history, a person of ordinary skill in the art would have understood the scope of the claims of the '350 patent to cover situations where, for example, the claimed pharmaceutical composition may comprise aripiprazole and an antidepressant in either a single or separate dosage forms. (See Declaration of Dr. Christoph U. Correll, M.D. ("Exhibit C") at ¶ 10.)

38. During this Court's Markman Hearing on October 19, 2015, Dr. Ira S. Halper, an expert for defendants in this and other related litigations, also confirmed that the inventive pharmaceutical composition of the '350 patent may comprise aripiprazole and an antidepressant in either a single or separate dosage forms. *See* Markman Transcript at 105:8-106:8 ("**Q**. So this passage means that the administration forms of the pharmaceutical composition of the present invention can be any type where Aripiprazole and an SRI are in the body at the same time. **A**. Yes. **Q**. And this passage indicates that the aripiprazole and the SRI may be in separate dosage forms. **A**. Yes.")

39. Upon information and belief, physicians, pharmacists and/or patients are directly infringing the '350 patent by the sale and use of Torrent Ltd.'s generic aripiprazole products in

combination with citalopram or escitalopram in accordance with the claims of the '350 patent. (Exhibit C at ¶ 10.)

40. Upon information and belief, Defendants have taken active steps to encourage the sale and use of Torrent Ltd.'s generic products by physicians, pharmacists and/or patients in accordance with the combination claimed in the '350 patent by providing information and instructions in package insert ("Exhibit D") encouraging the use of aripiprazole in combination with an antidepressant, including escitalopram. (Exhibit C at ¶¶ 12-13.)

41. Abilify® received approval for Adjunctive Treatment of Major Depressive Disorder ("MDD") in adults in November 2007. (Exhibit C at ¶ 14.)

42. At that time, revisions to the package insert for Abilify® were also approved by the FDA, which introduced new prescribing information specifically related to the use of Abilify® as an adjunct for treatment along with an antidepressant, such as escitalopram or citalopram, in accordance with the new indication. (Exhibit C at ¶¶ 14-15.)

43. Prior to the introduction of the new prescribing information related to the use of Abilify® for Adjunctive Treatment for Major Depressive Disorder, the package insert for Abilify® did not contain any information concerning prescribing and safety information regarding antidepressants, the use of Abilify® as an adjunct for treatment along with an antidepressant, any "Black Box" warning concerning antidepressants (i.e., suicidality), any information regarding MDD, any information regarding clinically important interactions between Abilify® and antidepressant drugs, for example escitalopram, or a "Medication Guide" for patients conveying the risk of Abilify® and antidepressant medications, nor did the package insert even mention the word "antidepressant." (Exhibit C at ¶ 15.)

44. The vast majority of the new prescribing information added to inform the reader about the use of Abilify® for Adjunctive Treatment of Major Depressive Disorder in the package insert for Abilify® has intentionally been included by Defendants in Defendants' package insert. (Exhibit C at ¶¶ 16-24.)

45. Defendants' package insert for Torrent Ltd.'s generic products includes prominent discussion of the use of antidepressants in the treatment for depression and MDD (using the word "antidepressant" over 30 times and using the terms "major depressive order" or "MDD" almost 10 times), and includes information about antidepressants in the "Black Box" warning section, about dosage and co-administration with escitalopram in the "Drug Interactions" section, and about the safety of antidepressants in the in the "Medication Guide" to patients section. (Exhibit D; Exhibit C at ¶ 16.)

46. The package insert for Torrent Ltd.'s generic products recommends, suggests, encourages and/or instructs physicians, pharmacists and/or patients to use Torrent Ltd.'s generic products in a manner that infringes at least one claim of the '350 patent by, for example:

- informing readers in the Black Box warning that no increase in risk of suicidality was observed in patients 24 and up taking antidepressants, and, in fact, that that there was a "reduction in risk" in patients aged 65 and older taking antidepressants, thus informing readers that there is significant benefit to the use of aripiprazole as an adjunct treatment with antidepressants (Exhibit C at ¶ 19, citing Defendants' package insert Exhibit D at pages 1-2);
- instructing readers in the "Drug Interactions" section that aripiprazole has no clinically important interactions with escitalopram and that no dosage adjustment is necessary when aripiprazole is coadministered with escitalopram, thus providing readers with

instructions regarding how aripiprazole may be administered in combination with escitalopram (Exhibit C at ¶ 20, citing Defendants' package insert Exhibit D at page 12);

— providing readers with safety instructions in Section 5.3 concerning the treatment of patients with major depressive disorder and of patients taking antidepressant medications (Exhibit C at ¶ 21, citing Defendants' package insert Exhibit D at pages 3);

— cautioning readers that "aripiprazole is not approved as a single agent for treatment of depression," thus indicating that aripiprazole can be used as an adjunct treatment for depression (Exhibit C at ¶ 22, citing Defendants' package insert Exhibit D at page 21); and by

— including a "Medication Guide" portion of the package insert for patients, which devotes almost two pages to side effects associated with antidepressants and treatment with aripiprazole (Exhibit C at ¶ 23, citing Defendants' package insert Exhibit D at pages 21-23).

47. Taken together, this information included in Defendants' package insert specifically informs the reader that aripiprazole may be used in treating depression as an adjunctive treatment and instructs the reader how aripiprazole may be safely coadministered with escitalopram, thus encouraging health care providers and others to use Torrent Ltd.'s generic aripiprazole products as an adjunct treatment for depression in combination with antidepressants, including escitalopram, in accordance with the claims of the '350 patent. (Exhibit C at ¶ 17.)

48. These same cited portions of the package insert were all originally added to the package insert for Abilify® specifically for the purpose of informing prescribers and patients about the use of Abilify® for Adjunctive Treatment of Major Depressive Disorder. (Exhibit C at ¶ 24.)

49. There would be no reason to include these portions of the package insert by Defendants other than to likewise have these portions considered by the reader for the purpose of providing information and instructions regarding the use of Torrent Ltd.'s generic aripiprazole products as an adjunct treatment with antidepressants in accordance with the '350 patent. (Exhibit C at ¶ 25.)

50. Upon information and belief, these portions of the package insert have intentionally been included by Defendants for that purpose. (Exhibit C at ¶ 24.)

51. Upon information and belief, Torrent Ltd. sells its own generic version of citalopram in connection with its ANDA No. 078216 and its own generic version of escitalopram in connection with its ANDA No. 090939.

52. Upon information and belief, Defendants' sale of their own generic versions of aripiprazole, citalopram and escitalopram further actively facilitates and encourages the use of Torrent Ltd.'s generic products by physicians, pharmacists and/or patients in accordance with the combination claimed in the '350 patent.

53. Abilify® is one of the largest selling drugs in the United States, with gross sales exceeding $7.5 billion in 2014.

54. Based on administrative claims data obtained from OptumHealth Reporting and Insights, approximately 16.5 to 21% of the total sales of aripiprazole are attributable to sales of aripiprazole as an adjunct to treatment with citalopram or escitalopram in accordance with the combination claimed in the '350 patent.

55. Upon information and belief, Defendants have knowledge of the high number of sales of aripiprazole as an adjunct to treatment with citalopram or escitalopram in accordance with the combination claimed in the '350 patent.

56. Upon information and belief, the active steps taken by Defendants as set forth above in paragraphs 31-55 to encourage the sale and use of Torrent Ltd.'s generic products in accordance with the combination claimed in the '350 patent by physicians, pharmacists and/or patients have been done with a specific intent to encourage infringement of the '350 patent in order to take advantage of these sales.

57. Upon information and belief, under 35 U.S.C. § 271(e)(2)(A), Defendants have infringed at least one claim of the '350 patent by submitting, or causing to be submitted to the FDA, ANDA No. 20-1519 seeking approval to manufacture, use, sell, offer to sell and import Torrent Ltd.'s generic products before the expiration date of the '350 patent, and by taking active steps to encourage the sale and use of Torrent Ltd.'s generic products in accordance with the combination claimed in the '350 patent by physicians, pharmacists and/or patients with the specific intent to encourage infringement of the '350 patent in order to take advantage of the large commercial market for such sales.

58. Upon information and belief, Torrent Ltd.'s actions relating to Torrent's ANDA No. 20-1519 complained of herein were done with the cooperation, participation and assistance, and for the benefit, of Torrent Inc., Torrent Ltd. and Hetero Labs Limited.

FOURTH COUNT FOR PATENT INFRINGEMENT

59. Otsuka realleges, and incorporates in full herein, paragraphs 17-22, 27-28 and 31-57.

60. Upon information and belief, Defendants are infringing at least one claim of the '350 patent under 35 U.S.C. § 271(b) by Defendants' manufacture, market, import, use, sale and offer for sale of Torrent Ltd.'s generic products, and by taking active steps to encourage the sale and use of Torrent Ltd.'s generic products in accordance with the combination claimed in

the ’350 patent by physicians, pharmacists and/or patients with the specific intent to encourage infringement of the ’350 patent in order to take advantage of the large commercial market for such sales.

WHEREFORE, Plaintiff Otsuka respectfully requests that the Court enter judgment in its favor and against Defendants on the patent infringement claims set forth above and respectfully requests that this Court:

1) enter judgment that, under 35 U.S.C. § 271 (e)(2)(A), Defendants have infringed at least one claim of the ’760 patent through Torrent Ltd.’s submission of ANDA No. 20-1519 to the FDA to obtain approval to manufacture, use, import, offer to sell and sell Torrent Ltd.’s generic products in the United States before expiration of the ’760 patent;

2) enter judgment that, under 35 U.S.C. § 271(a), the Defendants have infringed at least one claim of the ’760 patent through manufacture, market, import, use, sale and offer to sale of Torrent Ltd.’s generic products in the United States before the expiration of the ’760 patent;

3) enjoin Defendants from the manufacture, use, import, offer for sale and sale of Torrent Ltd.’s generic products until the expiration of the ’760 patent, or such later date as the Court may determine;

4) award Otsuka all available and legally permissible damages sufficient to compensate Otsuka for Defendants’ infringement of the ’760 patent, together with interest, in an amount to be determined at trial;

5) enter judgment that, under 35 U.S.C. § 271 (e)(2)(A), Defendants have infringed at least one claim of the ’350 patent through Torrent Ltd.’s submission of ANDA

No. 20-1519 to the FDA to obtain approval to manufacture, use, sell, offer to sell and import Torrent Ltd.'s generic products in the United States before expiration of the '350 patent;

6) enter judgment that, under 35 U.S.C. § 271(b), the Defendants have infringed at least one claim of the '350 patent through manufacture, market, import, use, sale and offer to sale of Torrent Ltd.'s generic products in the United States before the expiration of the '350 patent;

7) enjoin Defendants from the manufacture, use, sale, offer for sale and import of Torrent Ltd.'s generic products until the expiration of the '350 patent, or such later date as the Court may determine;

8) award Otsuka all available and legally permissible damages sufficient to compensate Otsuka for Defendants' infringement of the '350 patent, together with interest, in an amount to be determined at trial;

9) find Defendants' infringement to have been willful and award Otsuka enhanced damages for this willful infringement;

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

11) award Otsuka such further and additional relief as this Court deems just and proper.

Date: October 20, 2015

Respectfully submitted,

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