IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ONYX THERAPEUTICS, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. _____
	)	
DR. REDDY'S LABORATORIES, INC. and DR. REDDY'S LABORATORIES, LTD.,	)	
	)	
Defendants.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiff Onyx Therapeutics, Inc. ("Plaintiff" or "Onyx") brings this action for patent infringement against Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. (collectively, "Defendants" or "DRL").

THE PARTIES

1. Plaintiff Onyx is a corporation organized under the laws of the State of Delaware, having a principal place of business at One Amgen Center Drive, Thousand Oaks, California 91320-1799. Onyx is a wholly owned subsidiary of Onyx Pharmaceuticals, Inc. Onyx Pharmaceuticals, Inc. is a wholly owned subsidiary of Amgen Inc.

2. On information and belief, Defendant Dr. Reddy's Laboratories, Inc. is a corporation organized and existing under the laws of the State of New Jersey, having a principal place of business at 107 College Road East, Princeton, NJ 08540.

3. On information and belief, Defendant Dr. Reddy's Laboratories, Ltd. is an Indian corporation, having a principal place of business at 8-2-337, Road No. 3, Banjara Hills, Hyderabad, Telangana 500 034, India.

4. On information and belief, DRL has made or has caused to be made the proposed generic carfilzomib 60 mg lyophilized powder for reconstitution and for intravenous administration (the "Proposed ANDA Product") that is the subject of ANDA No. 209422and, through the filing of that ANDA with the U.S. Food and Drug Administration ("FDA") pursuant to 21 U.S.C. § 355(j) (Section 505(j) of the Federal Food, Drug and Cosmetic Act), seeks regulatory approval to market and sell the Proposed ANDA Product throughout the United States, including within this District.

5. On information and belief, Dr Reddy's Laboratories, Inc. is a wholly owned subsidiary of Dr. Reddy's Laboratories, Ltd., and is controlled by Dr. Reddy's Laboratories, Ltd.

6. On information and belief, Dr. Reddy's Laboratories, Inc. acts as the U.S. agent of Dr. Reddy's Laboratories, Ltd. with respect to ANDA No. 209422, and it will work, either directly or indirectly, to manufacture, import, market, and sell the Proposed ANDA Product.

7. On information and belief, Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. are in the business of, among other things, developing, preparing, manufacturing, selling, marketing, and distributing generic pharmaceutical products throughout the United States, including in the State of Delaware.

NATURE OF THE ACTION

8. This is a civil action for patent infringement under the patent laws of the United States, Title 35, United States Code, arising out of DRL's ANDA No. 209422, filed with the FDA seeking approval to engage in the commercial manufacture, use and sale of the Proposed ANDA Product prior to the expiration of U.S. Patent No. 7,737,112 ("the Patent-in-Suit"), which is owned by Onyx.

9. The Proposed ANDA Product is a generic version of Onyx's KYPROLIS® (carfilzomib) for injection.

JURISDICTION AND VENUE

10. This Court has jurisdiction over the subject matter of this action, which arises under the patent laws of the United States, pursuant to 28 U.S.C. §§ 1331 and 1338(a), and 35 U.S.C. § 1 et seq.

11. This Court has personal jurisdiction over Defendants because, on information and belief, Defendants directly or indirectly, manufacture, import, market, and sell generic drugs throughout the United States and in this judicial district.

12. On information and belief, Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. are working in concert for the purposes of developing, formulating, manufacturing, marketing, and selling drug products throughout the United States, including Delaware, and Delaware will be a destination of the Proposed ANDA Product.

13. This Court also has jurisdiction over Defendants because, *inter alia*, this action arises from actions of Defendants directed toward Delaware, and because Defendants have purposefully availed themselves of the rights and benefits of Delaware law by engaging in systematic and continuous contacts with Delaware. Upon information and belief, Defendants regularly and continuously transact business within Delaware, including by selling pharmaceutical products in Delaware, either on their own or through their affiliates. Upon information and belief, Defendants derive substantial revenue from the sale of those products in Delaware and have availed themselves of the privilege of conducting business within Delaware.

14. This Court has jurisdiction over Defendants because, *inter alia*, upon information and belief, Defendants have previously been sued in this judicial district without objecting on the

basis of lack of personal jurisdiction and have availed themselves of Delaware courts through the assertions of counterclaims in suits brought in Delaware. *See, e.g., Galderma Labs., LP et al. v. Dr. Reddy's Labs., Ltd. et al.*, Civil Action No. 15-670 (D. Del.); *Cephalon, Inc. v. Dr. Reddy's Labs., Ltd. et al.*, Civil Action No. 14-1241 (D. Del.). Upon information and belief, Defendants have previously submitted to the jurisdiction of this Court and have availed themselves of the legal protections of the State of Delaware by having filed suit in this jurisdiction. *See Dr. Reddy's Labs., Inc. et al. v. Fresenius Kabi USA, LLC*, Civil Action No. 15-714 (D. Del.).

15. In *Galderma Labs., LP et al. v. Dr. Reddy's Laboratories, Ltd. et al.*, Civil Action No. 15-670, D.I. 13 at ¶ 10 (D. Del.), both Dr. Reddy's Laboratories, Inc. and Dr. Reddy's Laboratories, Ltd. admitted that this Court has personal jurisdiction over Dr. Reddy's Laboratories, Inc.

16. Venue is proper in this District pursuant to 28 U.S.C. §§ 1391(b), (c) and 1400(b).

THE PATENT-IN-SUIT

17. United States Patent No. 7,737,112 (the "'112 Patent"), entitled "Compounds For Enzyme Inhibition," was duly and legally issued on June 15, 2010 and will expire on December 7, 2027. Onyx is the owner of the '112 Patent. A copy of the '112 Patent is attached as Exhibit A.

FACTUAL BACKGROUND

KYPROLIS® (CARFILZOMIB) FOR INJECTION

18. On July 20, 2012, the FDA granted accelerated approval to Onyx to market KYPROLIS® (carfilzomib) for injection to treat relapsed or refractory multiple myeloma, a type of cancer, and more specifically a type of hematopoietic cancer. Per the FDA, the accelerated approval program is designed to provide patients with earlier access to promising new drugs.

Previously, in January 2011, the FDA had granted KYPROLIS® (carfilzomib) for injection "Fast Track" designation, which is a unique FDA process designed to facilitate the development and expedite the review of drugs based on the FDA's determination that it has the potential to treat serious conditions and fill an unmet medical need.

19. As described in the FDA approved label for KYPROLIS® (carfilzomib) for injection, several clinical studies have established the drug's effectiveness for treating relapsed or refractory multiple myeloma. One such clinical study is the pivotal Phase 3 head-to-head ENDEAVOR study comparing KYPROLIS® (carfilzomib) for injection plus dexamethasone to VELCADE® (bortezomib) plus dexamethasone, which is a current standard of care in relapsed multiple myeloma. The data showed that patients treated with KYPROLIS® (carfilzomib) for injection plus dexamethasone achieved progression-free survival of 18.7 months compared to 9.4 months in those receiving VELCADE® (bortezomib) plus dexamethasone. Put differently, the ENDEAVOR study demonstrates that patients treated with KYPROLIS® (carfilzomib) for injection lived almost twice as long without disease worsening as those treated with VELCADE® (bortezomib).

20. KYPROLIS® (carfilzomib) for injection is approved by the FDA in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy; and as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy.

21. KYPROLIS® (carfilzomib) for injection is FDA approved for intravenous use. It is FDA approved as a lyophilized powder in a single-dose 30 mg or 60 mg vial. Each 30 mg vial contains 30 mg of carfilzomib, 1500 mg sulfobutylether beta-cyclodextrin, and 28.9 mg

anhydrous citric acid and sodium hydroxide for pH adjustment (target pH 3.5). Each 60 mg vial contains 60 mg of carfilzomib, 3000 mg sulfobutylether beta-cyclodextrin, 57.7 mg citric acid, and sodium hydroxide for pH adjustment (target pH 3.5). The FDA approved label for KYPROLIS® (carfilzomib) for injection, provides detailed instructions for reconstituting the lyophilized KYPROLIS® (carfilzomib) powder before injection, including reconstituting each vial by slowly injecting Sterile Water for Injection, USP through the stopper and directing the solution into the inside wall of the vial, then gently swirling and/or inverting the vial slowly for about one minute, or until complete dissolution.

22. Carfilzomib, the active ingredient in KYPROLIS® (carfilzomib) for injection, is a proteasome inhibitor. The proteasome is the cell's "garbage disposal"; it breaks down unneeded or damaged proteins for reuse in the cell. Carfilzomib, a tetrapeptide epoxyketone, inhibits proteasome function by irreversibly binding to the N-terminal threonine-containing active sites of the 20S proteasome, the proteolytic core particle within the 26S proteasome. This causes the accumulation of protein in multiple myeloma cells, which triggers the body's mechanisms to kill the multiple myeloma cell through a process called apoptosis. According to the FDA approved label for KYPROLIS® (carfilzomib) for injection, carfilzomib has antiproliferative and proapoptotic activities *in vitro* in solid and hematologic tumor cells. In animals, carfilzomib inhibits proteasome activity in blood and tissue and delays tumor growth in models of multiple myeloma, hematologic, and solid tumors.

23. Onyx is the holder of approved New Drug Application ("NDA") No. 20-2714 for KYPROLIS® (carfilzomib) for injection. Onyx is the authorized agent for matters related to NDA No. 20-2714 in the United States.

24. KYPROLIS® (carfilzomib) for injection is covered by one or more claims of the Patent-in-Suit, and the Patent-in-Suit has been listed for NDA No. 20-2714 in the FDA's

publication, *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is referred to as the "Orange Book."

25. Also listed for NDA No. 20-2714 in the Orange Book are U.S. Patent Nos. 7,417,042; 7,232,818; 7,491,704; 8,129,346; 8,207,125; 8,207,126; 8,207,127; and 8,207,297 ("the Orange Book Patents"), which are owned by Onyx. KYPROLIS® (carfilzomib) for injection, its active pharmaceutical ingredient carfilzomib, its method of manufacture, and use are covered by one or more claims of the Orange Book Patents. U.S. Patent Nos. 7,232,818; 7,491,704; 8,129,346; 8,207,125; 8,207,126; 8,207,127; and 8,207,297 will expire April 14, 2025, and U.S. Patent No. 7,417,042 will expire July 20, 2026.

26. Pursuant to NDA No. 20-2714, Onyx markets and distributes KYPROLIS® (carfilzomib) for injection in the United States.

DEFENDANTS' ANDA

27. On September 20, 2016, Onyx received a letter, dated September 19, 2016, from DRL notifying Onyx that DRL seeks through ANDA No. 209422 approval to engage in the commercial manufacture, use sale, and offer for sale of the Proposed ANDA Product prior to the expiration of the Patent-in-Suit. Included within ANDA No. 209422 is a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") that the Patent-in-Suit is invalid, unenforceable, and/or will not be infringed by the manufacture, use, importation, sale or offer for sale of the Proposed ANDA Product.

28. Onyx commenced this action within 45 days of receipt of the Notice Letter.

29. On information and belief, Dr. Reddy's Laboratories, Ltd. knowingly encouraged, directed, and actively induced Dr. Reddy's Laboratories, Inc. to file ANDA No. 209422 with a Paragraph IV Certification.

30. Defendants were aware of the Patent-in-Suit when ANDA No. 209422 was filed with a Paragraph IV Certification.

31. On information and belief, in ANDA No. 209422, DRL did not include a Paragraph IV Certification that the Orange Book Patents are invalid, unenforceable, and/or will not be infringed by the manufacture, use, importation, sale or offer for sale of the Proposed ANDA Product.

32. On information and belief, in ANDA No. 209422, DRL did include a Paragraph III certification that, if the Proposed ANDA Product is approved by the FDA, Defendants will not market it until the expiration of the Orange Book Patents.

33. On information and belief, carfilzomib is the active ingredient in the Proposed ANDA Product and is a proteasome inhibitor approved by the FDA in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy; and as a single agent for the treatment of patients with relapsed or refractory multiple myeloma who have received one or more lines of therapy. 21 U.S.C. § 355(j)(2); 21 C.F.R. § 314.94(a)(5).

34. On information and belief, ANDA No. 209422 refers to and relies upon the NDA for KYPROLIS® (carfilzomib) for injection and contains data that, according to Defendants, demonstrate the bioequivalence of the Proposed ANDA Product and KYPROLIS® (carfilzomib) for injection. 21 U.S.C. § 355(j)(2); 21 C.F.R. § 314.94(a)(7).

35. On information and belief, the Proposed ANDA Product will have instructions for use that substantially copy the instructions accompanying KYPROLIS® (carfilzomib) for injection, including instructions for administering the Proposed ANDA Product by intravenous injection to treat multiple myeloma in humans, as well as instructions for reconstituting the

Proposed ANDA Product before injection by slowly injecting Sterile Water for Injection, USP into each vial through the stopper and directing the solution into the inside wall of the vial, then gently swirling and/or inverting the vial slowly for about one minute, or until complete dissolution. 21 U.S.C. § 355(j)(2); 21 C.F.R. § 314.94(a)(4) and (8). The instructions accompanying the Proposed ANDA Product will induce healthcare providers to use the Proposed ANDA Product in a manner set forth in those instructions.

36. On information and belief, DRL intends to have healthcare providers use its Proposed ANDA Product, if approved, as set forth in its Proposed ANDA Product label. On information and belief, DRL's Proposed ANDA Product label instructs healthcare providers to administer its Proposed ANDA Product by intravenous injection to treat multiple myeloma in humans after reconstituting the Proposed ANDA Product by slowly injecting Sterile Water for Injection, USP into each vial through the stopper and directing the solution into the inside wall of the vial, then gently swirling and/or inverting the vial slowly for about one minute, or until complete dissolution. Thus, DRL knowingly intends to encourage healthcare providers to administer its ANDA Product by intravenous injection to treat multiple myeloma in humans in a manner that infringes the Patent-in-Suit.

37. On information and belief, the Proposed ANDA Product will have no substantial non-infringing use.

CLAIM FOR INFRINGEMENT OF U.S. PATENT NO. 7,737,112

38. Plaintiff hereby realleges and incorporates the allegations of paragraphs 1 – 37 of this Complaint.

39. On information and belief, the Proposed ANDA Product is covered by at least Claims 1-9, 14, 18-24, and 29-32 of the '112 Patent, because it contains carfilzomib, sulfobutyl

ether beta-cyclodextrin (SBECD), and citric acid. 21 C.F.R. § 314.127(a)(8)(ii)(B); 21 C.F.R. § 314.94(a)(9)(iii).

40. Defendants' submission of ANDA No. 209422 under 21 U.S.C. § 355(j) for the purpose of obtaining approval to engage in the commercial manufacture, use, importation, sale and/or offer for sale of the Proposed ANDA Product before the expiration of the '112 Patent constitutes infringement of the '112 Patent under 35 U.S.C. § 271(e)(2).

41. On information and belief, Defendants plan to, intend to, and will engage in the commercial manufacture, use, importation, sale and/or offer for sale of the Proposed ANDA Product immediately upon approval of ANDA No. 209422 and will instruct healthcare providers to use the Proposed ANDA Product in accordance with the proposed product labeling.

42. On information and belief, Defendants know that the Proposed ANDA Product, when commercially manufactured, offered for sale, sold, and/or imported, and when used, will directly infringe at least Claims 1-9, 14, 18-24, and 29-32 of the '112 Patent under 35 U.S.C. § 271(a).

43. Upon FDA approval of ANDA No. 209422, Defendants will infringe at least Claims 1-9, 14, 18-24, and 29-32 of the '112 Patent by making, using, offering to sell, selling, and/or importing the Proposed ANDA Product in the United States, and by actively inducing and/or contributing to infringement by others under 35 U.S.C. § 271(b) and/or (c).

44. On information and belief, Defendants had knowledge of the '112 Patent when Defendants submitted ANDA No. 209422 to the FDA and Defendants know or should know that they will induce or contribute to another's direct infringement of at least Claims 1-9, 14, 18-24, and 29-32 of the '112 Patent.

45. Absent from the Notice Letter are any allegations that Claims 1-9, 14, 18-24, or 29-32 of the ’112 Patent are not infringed by the Proposed ANDA Product.

46. Defendants have knowledge of the ’112 Patent and are knowingly and intentionally infringing the ’112 Patent.

47. Plaintiff will be substantially and irreparably harmed by the infringing activities described above unless those activities are enjoined by this Court. Plaintiff has no adequate remedy at law.

48. On information and belief, Defendants lacked a good faith basis for alleging invalidity of the ’112 Patent when Defendants filed their Paragraph IV Certification. Accordingly, this case is exceptional under 35 U.S.C. § 285.

PRAYER FOR RELIEF

WHEREFORE, Plaintiff respectfully requests that this Court grant the following relief:

a) Judgment that Defendants’ submission of ANDA No. 209422 to the FDA was an act of infringement of one or more Claims of the ’112 Patent under 35 U.S.C. § 271(e)(2);

b) Judgment that Defendants’ making, using, offering to sell, selling, or importing into the United States of the Proposed ANDA Product prior to the expiration of the ’112 Patent, will infringe, will actively induce infringement, and/or will contribute to the infringement of one or more Claims of that Patent;

c) An Order pursuant to 35 U.S.C. § 271(e)(4)(A) providing that the effective date of any FDA approval of ANDA No. 209422 shall be a date that is not earlier than the expiration of the ’112 Patent plus any other exclusivity to which Plaintiff is or becomes entitled;

d) An Order permanently enjoining Defendants, Defendants’ affiliates and subsidiaries, each of their officers, agents, servants and employees, and any person acting in

concert with Defendants, from making, using, offering to sell, selling, or importing into the United States the Proposed ANDA Product until after the expiration of the '112 Patent plus any other exclusivity to which Plaintiff is or becomes entitled;

e) A declaration that this case is exceptional within the meaning of 35 U.S.C. § 285 and an award of reasonable attorneys' fees, expenses, and disbursements of this action;

f) An award of Plaintiff's reasonable costs and expenses in this action; and

g) Such further and other relief as this Court deems proper and just.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Jack B. Blumenfeld

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