IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ZS PHARMA, INC. and ASTRAZENECA PHARMACEUTICALS LP,	)	
Plaintiffs,	)	C.A. No. _____
v.	)	
ASCENT PHARMACEUTICALS INC. and HETERO DRUGS LTD.,	)	
Defendants.	)	

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs ZS Pharma, Inc. and AstraZeneca Pharmaceuticals LP (collectively, "AstraZeneca" or "Plaintiffs") bring this action for patent infringement against Defendants Ascent Pharmaceuticals Inc. ("Ascent") and Hetero Drugs Ltd. ("Hetero," collectively with Ascent, "Defendants").

NATURE OF THE ACTION

1. This is a civil action for patent infringement arising under the patent laws of the United States, 35 U.S.C. § 1, *et seq.*, and in particular under 35 U.S.C. § 271. This action relates to Abbreviated New Drug Application ("ANDA") No. 217578, filed by and for the benefit of Defendants with the United States Food and Drug Administration ("FDA"). Through ANDA No. 217578, Defendants seek approval to market generic versions of LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet (the "Proposed ANDA Product"), prior to the expiration of U.S. Patent No. 11,738,044 ("the '044 Patent").

THE PARTIES

2. Plaintiff ZS Pharma, Inc. is a corporation organized and existing under the laws of Delaware, having a principal place of business in Wilmington, Delaware.

3. Plaintiff AstraZeneca Pharmaceuticals LP is a limited partnership organized and existing under the laws of Delaware, having a principal place of business in Wilmington, Delaware.

4. On information and belief, Defendant Ascent Pharmaceuticals Inc. 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.

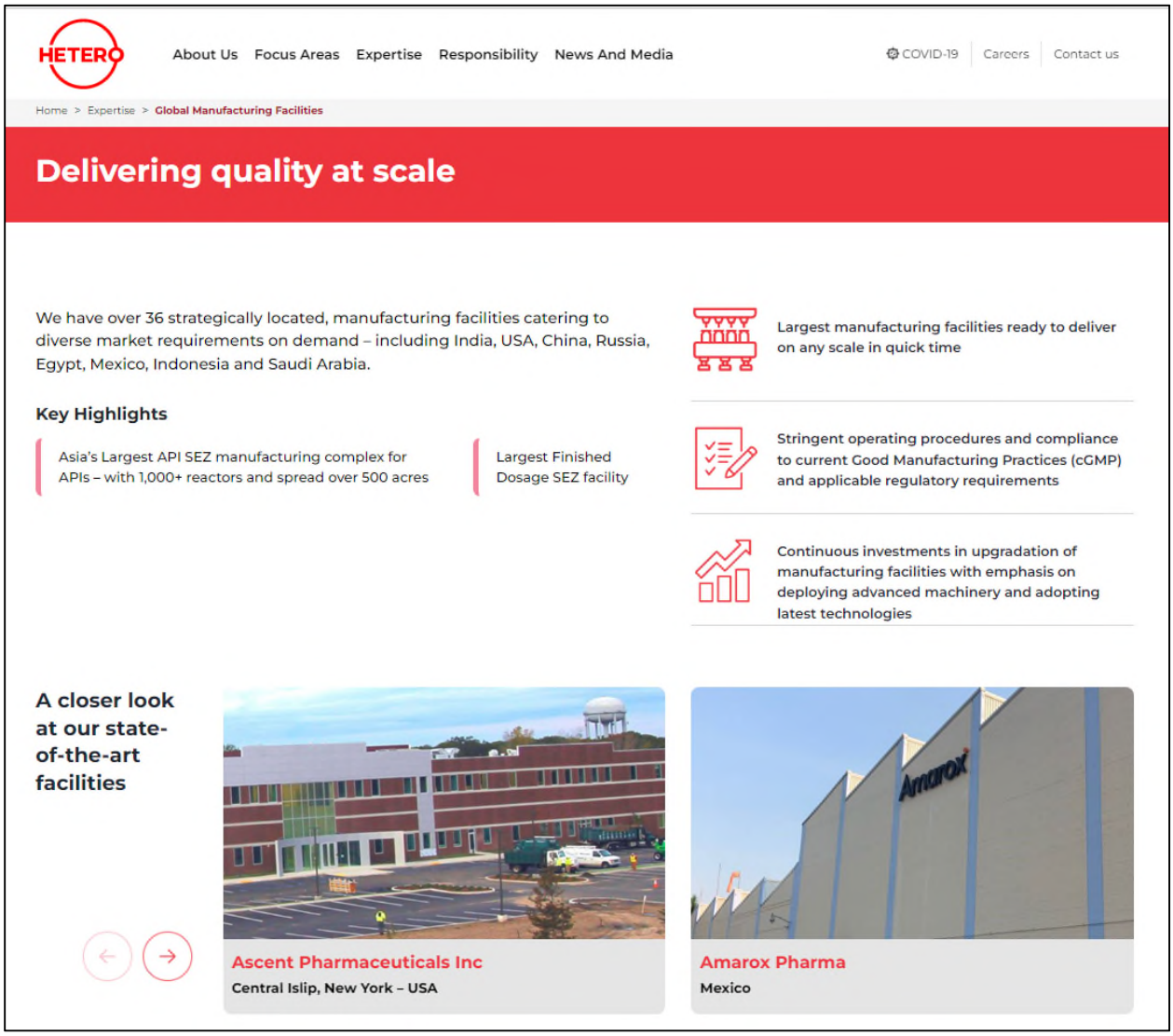
5. On information and belief, Defendant Hetero Drugs Ltd. is a corporation organized and existing under the laws of the Republic of India, having a principal place of business at 7-2-A2, Hetero Corporate Industrial Estates, Sanath Nagar, Hyderabad – 500 018, Telangana, India.

6. On information and belief, Defendants Ascent Pharmaceuticals Inc. and Hetero Drugs Ltd. hold themselves out as a unitary entity and operate as a single integrated business with respect to the regulatory approval, manufacturing, marketing, sale and distribution of generic pharmaceutical products throughout the United States, including in this judicial district.

7. On information and belief, Defendant Hetero Drugs Ltd. is one of the two flagship companies of the Hetero Group. *See* Exhibit B, https://www.hetero.com/who-we-are (stating that the Hetero Group "reach[es] out to the world through our flagship companies – Hetero Drugs Limited and Hetero Labs Limited across diverse businesses") (last accessed October 18, 2023). Of these flagship companies, Hetero Labs Limited is primarily engaged in the business of making drug product, while Hetero Drugs Ltd. is primarily engaged in the business of making active

pharmaceutical ingredient. *See* Exhibit C, December 7, 2021 Press Release of CARE Ratings Limited for Hetero Labs Limited at Page 2.

8. On information and belief, Defendant Ascent Pharmaceuticals Inc. is a member of the Hetero Group. The Hetero Group touts its vertical integration of global manufacturing facilities, with "over 36 strategically located, manufacturing facilities catering to diverse market requirements on demand . . . .":



See Exhibit D, https://www.hetero.com/global-manufacturing-facilities (last assessed October 18, 2023). The Hetero Group lists Defendant Ascent Pharmaceuticals Inc. among its manufacturing

facilities. *Id.*; *see also* Exhibit E, August 2017 Press Release of Camber Pharmaceuticals, Inc. ("With more than 25 manufacturing facilities around the world, including 5 plants in special economic zones, Hetero can produce more than 50 billion oral doses annually. . . . In the United States, Hetero has built a new 310,000-square-foot, state-of-the-art manufacturing facility in Central Islip, New York, on Long Island, for Camber's sister company, Ascent Pharmaceuticals, which opened in June 2017.").

9. On information and belief, Defendant Ascent Pharmaceuticals Inc. is affiliated with and majority owned by Hetero Labs Limited. *See* Exhibit C, December 7, 2021 Press Release of CARE Ratings Limited for Hetero Labs Limited at Page 5.

10. Defendants' ANDA No. 217578 seeks approval to commercially manufacture, use, offer for sale, sell, and/or import a generic version of AstraZeneca's LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet prior to the expiration of the '044 Patent.

11. On information and belief, Defendants' ANDA No. 217578 references a Drug Master File for sodium zirconium cyclosilicate held by Hetero Drugs Ltd.

12. On information and belief, Defendant Hetero Drugs Ltd. will supply the active pharmaceutical ingredient for Defendant Ascent Pharmaceuticals Inc.'s Proposed ANDA Product. *See* Exhibit C, December 7, 2021 Press Release of CARE Ratings Limited for Hetero Labs Limited at Page 2 ("For procurement of [active pharmaceutical ingredient] required for manufacture of finished dosages; [Hetero Labs Limited] would continue to be dependent on its associate concerns particularly [Hetero Drugs Ltd.] . . . .").

13. On information and belief, Defendants collaborate with respect to the development, regulatory approval, marketing, sale, and/or distribution of pharmaceutical products. *See* Exhibit

C, December 7, 2021 Press Release of CARE Ratings Limited for Hetero Labs Limited at 2 ("[Hetero Labs Limited] procures raw materials i.e. APIs and intermediates from its group companies. The group has established various backward integrated units. During FY21, around 40 percent of the total raw materials were procured from its group companies (subsidiaries/associates and the companies on which key management personnel of [Hetero Labs Limited] can exercise significant influence) out of which, Hetero Drugs Ltd (HDL) . . . were the major contributors."). On further information and belief, Defendants are agents of each other and/or operate in concert as integrated parts of the same business group.

14. On information and belief, Defendants acted in concert to develop the Proposed ANDA Product that is the subject of ANDA No. 217578 and to seek regulatory approval from the FDA to market and sell the Proposed ANDA Product throughout the United States, including within this District.

15. On information and belief, Defendants intend to act collaboratively to obtain approval for Defendants' ANDA No. 217578, and, in the event the FDA approves that ANDA, to commercially manufacture, use, offer for sale, sell, and/or import the Proposed ANDA Product.

JURISDICTION AND VENUE

16. This is an action for patent infringement under the patent laws of the United States, Title 35, United States Code, arising out of the submission of Defendants' ANDA No. 217578 to the FDA.

17. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a), and 35 U.S.C. § 1 et seq.

18. This Court has personal jurisdiction over Defendants because, inter alia, they have maintained continuous and systematic contacts with this District and availed themselves of the

privilege of doing business in this District. On information and belief, Defendants: (1) acted in concert to file ANDA No. 217578 seeking approval to commercially manufacture, use, offer for sale, sell, and/or import the Proposed ANDA Product in the United States, including in this District; (2) regularly and continuously transacted business within this District, including by selling pharmaceutical products in this District either on their own or through their affiliates; and (3) derived substantial revenue from the sale of those products in this District. Alternatively, this Court has personal jurisdiction over Hetero pursuant to Federal Rule of Civil Procedure 4(k)(2).

19. On information and belief, if ANDA No. 217578 is approved, the Proposed ANDA Product accused of infringing the '044 Patent will be marketed, distributed, offered for sale, and/or sold in this District, prescribed by physicians practicing in this District, dispensed by pharmacies located within this District, and/or used by patients in this District, all of which would have a substantial effect on this District.

20. This Court also has personal jurisdiction over Defendants because they have affirmatively availed themselves of the jurisdiction of this Court through the assertion of counterclaims in suits brought in this District and/or by being sued in this District without challenging personal jurisdiction. *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.); *Duchesnay Inc. et al. v. Hetero Labs Limited*, 21-1130 (D. Del.); *Otsuka Pharmaceutical Co., Ltd. et al. v. Hetero Labs, Ltd.*, 20-cv-1531 (D. Del.).

21. This Court also has personal jurisdiction over Ascent at least because Ascent has confirmed that it will not contest personal jurisdiction in this District for purposes of litigation involving ANDA No. 217578. Ascent did not contest this Court's jurisdiction in Plaintiffs' previously-filed civil action regarding Defendants' ANDA No. 217578, Civil Action No. 22-1099-

GBW. *See ZS Pharma, Inc. et al. v. Ascent Pharmaceuticals Inc. et al.*, Civil Action No. 22-1099-GBW, D.I. 19 at ¶¶ 18, 21, 22 (D. Del.). For the reasons set forth above, and for additional reasons which will be supplied if Defendants challenge personal jurisdiction in this action, Defendants are subject to personal jurisdiction in this District.

22. Venue is proper in this District for Ascent at least because Ascent has confirmed that it will not contest venue in this District for purposes of litigation involving ANDA No. 217578. Ascent did not contest venue in this District in Plaintiffs' previously-filed civil action regarding Defendants' ANDA No. 217578, Civil Action No. 22-1099-GBW. *See ZS Pharma, Inc. et al. v. Ascent Pharmaceuticals Inc. et al.*, Civil Action No. 22-1099-GBW, D.I. 19 at ¶ 23 (D. Del.).

23. Venue is proper in this District for Hetero pursuant to 28 U.S.C. § 1391(c) because, *inter alia*, Hetero is a corporation organized and existing under the laws of the Republic of India and is subject to personal jurisdiction in this District.

THE '044 PATENT

24. The '044 Patent is assigned to ZS Pharma, Inc.

25. The '044 Patent, entitled "Extended Use Zirconium Silicate Compositions and Methods of Use Thereof," was duly and legally issued on August 29, 2023. A copy of the '044 Patent is attached as Exhibit A.

FACTUAL BACKGROUND

LOKELMA® (sodium zirconium cyclosilicate)

26. LOKELMA® (sodium zirconium cyclosilicate) is a drug used to treat hyperkalemia. Marked elevations in serum potassium can cause fatal heart arrhythmias and abnormalities in conduction (progression of electrical impulses through the heart) and muscle weakness and paralysis. LOKELMA® (sodium zirconium cyclosilicate) is a non-absorbed zirconium silicate that

preferentially captures potassium in exchange for hydrogen and sodium, thereby lowering serum potassium levels.

27. AstraZeneca is the holder of approved New Drug Application ("NDA") No. 207078 for LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet. Pursuant to NDA No. 207078, AstraZeneca markets and distributes LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet in the United States.

28. LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet, the active pharmaceutical ingredient sodium zirconium cyclosilicate, the method of manufacture, and/or their use are covered by one or more claims of the '044 Patent. The '044 Patent has been listed for NDA No. 207078 in the FDA publication *Approved Drug Products with Therapeutic Equivalence Evaluations*, which is also known as the "Orange Book."

Defendants' ANDA No. 217578

29. In a letter dated July 18, 2022 (the "Notice Letter"), Defendants stated that they had submitted ANDA No. 217578 to the FDA seeking approval to commercially manufacture, use, offer for sale, sell, and/or import the Proposed ANDA Product. The Notice Letter further stated that ANDA No. 217578 contained a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) (a "Paragraph IV Certification") that U.S. Patent Nos. 8,802,152 ("the '152 Patent"), 8,808,750 ("the '750 Patent"), 8,877,255 ("the '255 Patent"), 9,592,253 ("the '253 Patent"), 9,844,567 ("the '567 Patent"), 9,861,658 ("the '658 Patent"), 9,913,860 ("the '860 Patent"), 10,300,087 ("the '087 Patent"), 10,335,432 ("the '432 Patent"), 10,398,730 ("the '730 Patent"), 10,413,569 ("the '569 Patent"), and 10,695,365 ("the '365 Patent") are invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, offer for sale, sale, and/or importation of the Proposed ANDA Product. Plaintiffs timely filed suit with respect to those patents on August 22,

2022. *See ZS Pharma, Inc. et al. v. Ascent Pharmaceuticals Inc. et al.*, Civil Action No. 22-1099-GBW, D.I. 1 (D. Del.).

30. On information and belief, Defendants have amended or will amend ANDA No. 217578 to include a Paragraph IV Certification that U.S. Patent No. 11,406,662 ("the '662 Patent") is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, offer for sale, sale, and/or importation of the Proposed ANDA Product. Plaintiffs filed suit with respect to the '622 Patent on October 5, 2022. *See ZS Pharma, Inc. et al. v. Ascent Pharmaceuticals Inc. et al.*, Civil Action No. 22-1099-GBW, D.I. 15 (D. Del.).

31. On information and belief, Defendants have amended or will amend ANDA No. 217578 to include a Paragraph IV Certification that the '044 Patent is invalid, unenforceable, and/or will not be infringed by the commercial manufacture, use, offer for sale, sale, and/or importation of the Proposed ANDA Product.

32. Defendants' submission of ANDA No. 217578 to the FDA constitutes infringement of one or more claims of the '044 Patent under 35 U.S.C. § 271(e)(2)(A). Although the '044 Patent did not issue until after ANDA No. 217578 was filed, this does not preclude Defendants from infringement liability under 35 U.S.C. § 271(e)(2). *See Vanda Pharms. Inc. v. W.-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1127 (Fed. Cir. 2018).

33. On information and belief, sodium zirconium cyclosilicate is the active ingredient in the Proposed ANDA Product.

34. On information and belief, the Proposed ANDA Product exhibits sodium zirconium cyclosilicate as patented by the '044 Patent.

35. On information and belief, ANDA No. 217578 refers to and relies upon the NDA for LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per

packet and contains data that, according to Defendants, demonstrate the bioequivalence of the Proposed ANDA Product and LOKELMA® (sodium zirconium cyclosilicate) for oral suspension 5 g per packet and 10 g per packet. *See* 21 U.S.C. § 355(j)(2); 21 C.F.R. § 314.94(a)(7).

36. On information and belief, Defendants intend to have healthcare providers use their Proposed ANDA Product, if approved, as set forth in the Proposed ANDA Product label.

37. On information and belief, Defendants' Proposed ANDA Product label will instruct healthcare providers to prescribe the Proposed ANDA Product in the manner set forth in the label.

38. On information and belief, the FDA has not yet approved ANDA No. 217578.

COUNT I: INFRINGEMENT OF U.S. PATENT NO. 11,738,044

39. Plaintiffs hereby reallege and incorporate the allegations of paragraphs 1 – 38 of this Complaint.

40. On information and belief, the Proposed ANDA Product infringes one or more claims of the '044 Patent, either literally or under the doctrine of equivalents, by the use and/or presence in the Proposed ANDA Product of a sodium zirconium cyclosilicate as covered by one or more of the claims of the '044 Patent.

41. Defendants' submission of ANDA No. 217578 to the FDA under 21 U.S.C. § 355(j) for the purpose of obtaining approval to commercially manufacture, use, offer for sale, sell, and/or import the Proposed ANDA Product before the expiration of the '044 Patent constitutes infringement of the '044 Patent under 35 U.S.C. § 271(e)(2).

42. On information and belief, Defendants plan to, intend to, and will commercially manufacture, use, offer for sale, sell, and/or import the Proposed ANDA Product immediately upon approval of ANDA No. 217578 and will instruct healthcare providers to use the Proposed ANDA Product in accordance with the proposed product labeling.

43. On information and belief, upon FDA approval of ANDA No. 217578, Defendants will infringe the ’044 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 have or will have knowledge that if they were to receive approval from the FDA to market the Proposed ANDA Product described in ANDA No. 217578 and make the Proposed ANDA Product available for sale and/or use by others, e.g., by doctors, pharmacists, healthcare providers and patients, according to the package insert and prescribing information during the proposed shelf life of the products before expiration of the ’044 Patent, such activities would result in the sale and/or use of a product that itself infringes and/or is especially made for an infringing use. Upon information and belief, Defendants have or will have knowledge of such infringement and/or such infringing use and also knows or will know that the Proposed ANDA Product described in ANDA No. 217578 are not a staple article or commodity of commerce suitable for substantial non-infringing use, but rather are especially made to infringe and/or are especially adapted for use in the direct infringement of the ’044 Patent.

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

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs respectfully request that this Court grant the following relief:

a) Judgment that Defendants’ submission of ANDA No. 217578 to the FDA was an act of infringement of one or more claims of the ’044 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 '044 Patent, will infringe, will actively induce infringement, and/or will contribute to the infringement of one or more claims of the '044 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. 217578 shall be a date that is not earlier than the expiration of the '044 Patent plus any other exclusivity to which Plaintiffs are or become 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 '044 Patent plus any other exclusivity to which Plaintiffs are or become 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 Plaintiffs' reasonable costs and expenses in this action; and

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

DATED: October 20, 2023

MCCARTER & ENGLISH, LLP

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