**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF DELAWARE**

| | | |
|---|---|---|
| VERTEX PHARMACETUICALS INCORPORATED,<br><br>Plaintiffs,<br><br>v.<br><br>LUPIN LIMITED and LUPIN PHARMACEUTICALS, INC,<br><br>Defendants. | ) | C.A. No. 1:25-cv-00450 |

**LUPIN LIMITED AND LUPIN PHARMACEUTICALS, INC.'S ANSWER, AFFIRMATIVE DEFENSES, AND COUNTERCLAIMS TO PLAINTIFF'S COMPLAINT**

Defendants Lupin Limited ("Lupin Ltd.") and Lupin Pharmaceuticals, Inc. ("Lupin Pharmaceuticals") (collectively, "Defendants"), by and through their counsel, hereby answer and respond to each of the allegations in the Complaint by Vertex Pharmaceuticals Inc. ("Vertex" or "Plaintiff"), and assert their separate defenses, and Lupin Ltd. asserts its separate counterclaims, as follows.

**GENERAL DENIAL**

Pursuant to Federal Rule of Civil Procedure 8(b)(3), Defendants deny all allegations in Plaintiff's Complaint except those expressly admitted below

**NATURE OF THE ACTION**

1. This is a civil action for patent infringement under the patent laws of the United States, Title 35 of the United States Code, and the Declaratory Judgment Act, 28 U.S.C. § 2201, *et seq.*, arising from Defendant Lupin Limited's submission of Abbreviated New Drug Application ("ANDA") No. 217431 to the United States Food and Drug Administration ("FDA"), seeking approval to market a generic version of Vertex's KALYDECO® (ivacaftor) oral granules prior to the expiration of patents that cover, *inter alia*, KALYDECO® and its use.

**ANSWER:** The allegations in paragraph 1 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that the Complaint purports to state a claim for patent infringement under the patent laws of the United States, Title 35 of the United States Code, and the Declaratory Judgment Act, 28 U.S.C. § 2201. Defendants further admit that Lupin Ltd., as the sole applicant, submitted Abbreviated New Drug Application ("ANDA") No. 217431 to the U.S. Food and Drug Administration ("FDA") under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor oral granules described in ANDA No. 217431. Defendants further admit that ANDA No. 217431 includes certifications pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV) ("Paragraph IV Certification") with respect to U.S. Patent Nos. 8,883,206 ("the '206 patent"), 10,272,046 ("the '046 patent"), and 10,646,481 ("the '481 patent"), was amended on April 25, 2023 to include a Paragraph IV Certification with respect to U.S. Patent Nos. 11,564,916 ("the '916 patent"), was amended on February 27, 2024 to include a Paragraph IV Certification with respect to U.S. Patent No. 11,752,106 ("the '106 patent"), and was amended on March 19, 2025 to include a Paragraph IV Certification with respect to U.S. Patent No. 12,214,083 ("the '083 patent"). Defendants deny all other allegations in paragraph 1.

2. In ANDA No. 217431, Defendant Lupin Limited seeks approval to commercially market a generic version of Vertex's KALYDECO® prior to the expiration of United States Patent Nos. 8,883,206 (the "'206 patent"), 10,272,046 (the "'046 patent"), 10,646,481 (the "'481 patent"), 11,147,770 (the "'770 patent"), 11,564,916 (the "'916 patent"), 11,752,106 ("the '106 patent"), and 12,214,083 ("the '083 patent"), which are owned by Vertex.

**ANSWER:** Defendants admit that Lupin Ltd., as the sole applicant, submitted ANDA No. 217431 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor oral granules described in ANDA No. 217431. Defendants further admit that ANDA No. 217431 includes Paragraph IV Certifications with respect to the '206, '046, and '481 patents, was amended on April 25, 2023 to include a Paragraph IV Certification with Respect to the '916 patent, was amended on February 27, 2024 to include a Paragraph IV Certification with respect to the '106 patent, and was

amended on March 19, 2025 to include a Paragraph IV Certification with respect to the '083 patent. Defendants further aver that the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations* ("Orange Book") lists 04/14/2022 as the Submission Date for U.S. Patent No. 11,147,770 ("the '770 patent") in connection with NDA No. 207925, KALYDECO® (ivacaftor) granules, 25 mg/packet, 50 mg/packet, and 75 mg/packet and that ANDA No. 217431 did not include a Paragraph IV Certification with respect to the '770 patent. Defendants further admit that the '206, '046, '481, '770, '916, '106, and '083 patents list Vertex as the Assignee. Defendants deny all other allegations in paragraph 2.

3. On July 22, 2022, Vertex brought an action against Lupin for infringement of the '206, '046, '481, and '770 patents (C.A. No. 1:22-cv-00966-RGA) ("First Action").

**ANSWER:** Admitted.

4. On May 26, 2023, Vertex brought a separate action against Lupin for infringement of the '916 patent, arising from the amendment of ANDA No. 217431 (C.A. No. 1:23-cv-00583-RGA) ("Second Action").

**ANSWER:** Admitted.

5. On July 10, 2023, the First Action and Second Action were consolidated for all purposes including trial under C.A. No. 1:22-cv-00966-RGA.

**ANSWER:** Admitted.

6. On April 11, 2024, Vertex brought a separate action against Lupin for infringement of the '106 patent, arising from the further amendment of ANDA No. 217431 (C.A. No. 1:24-cv-00458-RGA) ("Third Action"). The Third Action was consolidated with Civil Action No. 1:22-cv-00966-RGA for all purposes including trial on May 23, 2024.

**ANSWER:** Admitted.

## THE PARTIES

7. Plaintiff Vertex is a corporation organized and existing under the laws of Massachusetts with its principal place of business at 50 Northern Avenue, Boston, MA 02210. Vertex is a biopharmaceutical company committed to improving the lives of patients worldwide. Vertex focuses on the pursuit of medical research to create transformative medicines for people with serious and life-threatening diseases, such as cystic fibrosis.

**ANSWER:** Defendants lack knowledge or information sufficient to form a belief about the truth of the allegations in paragraph 7 and therefore deny them.

8. Upon information and belief, Defendant Lupin Limited is a corporation organized and existing under the laws of India, with its principal place of business at 3rd Floor, Kalpataru Inspire, Off. Western Expressway Highway, Santacruz (East), Mumbai 400 055, India.

**ANSWER:** Admitted.

9. Upon information and belief, Defendant Lupin Pharmaceuticals, Inc. is a corporation organized and existing under the laws of Delaware, with its registered office at 5801 Pelican Bay Blvd., Suite 500, Naples, FL 34108-2734. Defendant Lupin Pharmaceuticals, Inc. is a wholly owned subsidiary of Lupin Limited.

**ANSWER:** Defendants admit that Lupin Pharmaceuticals is a corporation organized and existing under the laws of Delaware. The principal place of business of Lupin Pharmaceuticals is at 5801 Pelican Bay Blvd., Suite 500, Naples, FL 34108-2734. The allegations in the second sentence of paragraph 9 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Pharmaceuticals is an indirect, wholly owned subsidiary of Lupin Ltd. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 9.

10. Upon information and belief, Defendant Lupin Limited is in the business of, among other things, marketing and selling generic copies of branded pharmaceutical products for the United States market, alone and/or through its wholly owned subsidiaries and agents, including Defendant Lupin Pharmaceuticals, Inc.

**ANSWER:** Defendants admit that Lupin Ltd. manufactures pharmaceutical products, including generic pharmaceutical products. Defendants further admit that Lupin Pharmaceuticals distributes pharmaceutical products, including generic pharmaceutical products, in the United States. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 10.

## THE '083 PATENT

11. On February 4, 2025, the United States Patent and Trademark Office duly and legally issued the '083 patent, entitled "Pharmaceutical Composition and Administrations Thereof," to Vertex as assignee. A copy of the '083 patent is attached to this Complaint as Exhibit A.

**ANSWER:** The allegations in paragraph 11 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that the '083 patent is titled "Pharmaceutical Composition and Administrations Thereof" and lists February 4, 2025 as the Date of Patent. Defendants further admit that the '083 patent lists Vertex as the Assignee. Defendants further admit that, on information and belief, what purports to be a copy of the '083 patent is attached to the Complaint as Exhibit A. Defendants deny all other allegations in paragraph 11.

12. Vertex is the lawful owner of and holds all right, title, and interest in the '083 patent.

**ANSWER:** The allegations in paragraph 12 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that the '083 patent lists Vertex as the Assignee. Defendants deny all other allegations in paragraph 12.

## KALYDECO®

13. Vertex holds approved New Drug Application ("NDA") No. 207925 ("Vertex's NDA") for the use of ivacaftor 5.8, 13.4, 25, 50, and 75 mg oral granules ("Vertex's NDA Products") for the treatment of cystic fibrosis ("CF") in patients age one month to less than 6 years old who have at least one mutation in the cystic fibrosis transmembrane conductance regulator ("CFTR") gene that is responsive to ivacaftor based on clinical and/or *in vitro* assay data. Vertex sells the ivacaftor oral granules under the trade name KALYDECO®.

**ANSWER:** Defendants admit that the FDA's Orange Book lists "IVACAFTOR" as the Active Ingredient, "5.8MG/PACKET", "13.4MG/PACKET", "25MG/PACKET," "50MG/PACKET," or "75MG/PACKET" as the Strength, "VERTEX PHARMACEUTICALS INC" as the Applicant Holder, and "KALYDECO" as the Proprietary Name in connection with New Drug Application

("NDA") No. 207925. Defendants further admit on information and belief that the prescribing information for KALYDECO®, revised 08/2023, states, in part:

**1 INDICATIONS AND USAGE**
KALYDECO is indicated for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have at least one mutation in the *CFTR* gene that is responsive to ivacaftor potentiation based on clinical and/or *in vitro* assay data *[see Clinical Pharmacology (12.1) and Clinical Studies (14)]*.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a *CFTR* mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

Defendants lack knowledge or information sufficient to form a belief about the truth of all other allegations in paragraph 13 and therefore deny them.

14. Pursuant to 21 U.S.C. § 355(c)(2), and attendant FDA regulations, the '083 patent is listed in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations" (the "Orange Book"), with respect to Vertex's NDA.

**ANSWER:** The allegations in paragraph 14 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that the FDA's Orange Book lists the '083 patent in connection with NDA No. 207925, KALYDECO® (ivacaftor) granules, 5.8 mg/packet, 13.4 mg/packet, 25 mg/packet, 50 mg/packet, and 75 mg/packet. Defendants further admit that the FDA's Orange Book lists 02/21/2025 as the Submission Date for the '083 patent in connection with NDA No. 207925, KALYDECO® (ivacaftor) granules, 5.8 mg/packet, 13.4 mg/packet, 25 mg/packet, 50 mg/packet, and 75 mg/packet. Defendants deny all other allegations in paragraph 14.

## LUPIN'S ANDA

15. Upon information and belief, Defendant Lupin Limited acted in concert with Defendant Lupin Pharmaceuticals, Inc. to prepare and submit Abbreviated New Drug Application ("ANDA") No. 217431 ("Lupin's ANDA") to the FDA. Defendants submitted Lupin's ANDA, pursuant to 21 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture, use, sale, offer for sale, and/or importation of 25, 50, and 75 mg ivacaftor oral granules ("Lupin's ANDA Products"), which are based on Vertex's NDA Products, before the expiration of the '206, '046, '481, '770, '916, '106, and '083 patents.

**ANSWER:** The allegations in paragraph 15 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Ltd. submitted ANDA

No. 217431 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor granules described in ANDA No. 217431. Defendants further admit that ANDA No. 217431 includes Paragraph IV Certifications with respect to the '206, '046, and '481 patents, was amended on April 25, 2023 to include a Paragraph IV Certification with Respect to the '916 patent, was amended on February 27, 2024 to include a Paragraph IV Certification with respect to the '106 patent, and was amended on March 19, 2025 to include a Paragraph IV Certification with respect to the '083 patent. Defendants further aver that the FDA's Orange Book lists 04/14/2022 as the Submission Date for the '770 patent in connection with NDA No. 207925, KALYDECO® (ivacaftor) granules, 25 mg/packet, 50 mg/packet, and 75 mg/packet and that ANDA No. 217431 did not include a Paragraph IV Certification with respect to the '770 patent. Defendants further aver that the FDA's Orange Book lists 05/30/2023 as the Submission Date for the '770 patent in connection with NDA No. 207925, KALYDECO® (ivacaftor) granules, 5.8 mg/packet and 13.4 mg/packet. Defendants deny all other allegations in paragraph 15.

16. Upon information and belief, Lupin's ANDA refers to and relies upon Vertex's NDA and contains data that, according to Defendant Lupin Limited, demonstrates the bioequivalence of Lupin's ANDA Products to Vertex's NDA Products.

**ANSWER:** Defendants admit that ANDA No. 217431 identifies NDA No. 207925 and KALYDECO® (ivacaftor) granules, 25 mg/packet, 50 mg/packet, and 75 mg/packet as the Reference Listed Drug. Defendants further admit that ANDA No. 217431 contains information intended to establish bioequivalence with the Reference Listed Drug. Defendants deny all other allegations in paragraph 16.

17. By letter to Vertex dated June 9, 2022 ("Lupin's June 9, 2022 Paragraph IV Notice Letter"), Defendant Lupin Limited stated that Lupin's ANDA contained a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that no valid claim of the '206, '046, and '481 patents will be infringed by the manufacture, importation, use, or sale of Lupin's ANDA Products (the "June 9, 2022 Paragraph IV Certification"). Defendant Lupin Limited attached an exhibit to its June 9, 2022 letter, in which it purported to allege the factual and legal bases for its June 9, 2022 Paragraph IV Certification.

**ANSWER:** Defendants admit that Lupin Ltd. transmitted a letter dated June 9, 2022 ("First Notice Letter") to Plaintiff, notifying Plaintiff that Lupin Ltd. submitted ANDA No. 217431 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor granules described in ANDA No. 217431 and that ANDA No. 217431 includes Paragraph IV Certifications with respect to the '206, '046, and '481 patents. Defendants further admit that Lupin Ltd.'s First Notice Letter included a detailed statement of the factual and legal bases upon which Lupin Ltd. based its Paragraph IV Certifications with respect to the '206, '046, and '481 patents. Defendants deny all other allegations in paragraph 17.

18. By letter to Vertex dated April 25, 2023 ("Lupin's April 25, 2023 Paragraph IV Notice Letter"), Defendant Lupin Limited stated that Lupin's ANDA contained a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that no valid claim of the '916 patent will be infringed by the manufacture, importation, use, or sale of Lupin's ANDA Products (the "April 25, 2023 Paragraph IV Certification"). Defendant Lupin Limited attached an exhibit to its April 25, 2023 letter, in which it purported to allege the factual and legal bases for its April 25, 2023 Paragraph IV Certification.

**ANSWER:** Defendants admit that Lupin Ltd. transmitted a letter dated April 25, 2023 ("Second Notice Letter") to Plaintiff, notifying Plaintiff that Lupin Ltd., as the sole applicant, amended ANDA No. 217431 to include a Paragraph IV Certification with respect to the '916 patent. Defendants further admit that Lupin Ltd.'s Second Notice Letter included a detailed statement of the factual and legal bases upon which Lupin Ltd. based its Paragraph IV Certification with respect to the '916 patent. Defendants deny all other allegations in paragraph 18.

19. By letter to Vertex dated February 27, 2024 ("Lupin's February 27, 2024 Paragraph IV Notice Letter"), Defendant Lupin Limited stated that Lupin's ANDA contained a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that no valid claim of the '106 patent will be infringed by the manufacture, importation, use, or sale of Lupin's ANDA Products (the "February 27, 2024 Paragraph IV Certification"). Defendant Lupin Limited attached an exhibit to its February 27, 2024 letter, in which it purported to allege the factual and legal bases for its February 27, 2024 Paragraph IV Certification.

**ANSWER:** Defendants admit that Lupin Ltd. transmitted a letter dated February 27, 2024 ("Third Notice Letter") to Plaintiff, notifying Plaintiff that Lupin Ltd., as the sole applicant,

amended ANDA No. 217431 to include a Paragraph IV Certification with respect to the '106 patent. Defendants further admit that Lupin Ltd.'s Third Notice Letter included a detailed statement of the factual and legal bases upon which Lupin Ltd. based its Paragraph IV Certification with respect to the '106 patent. Defendants deny all other allegations in paragraph 19.

20. By letter to Vertex dated March 19, 2025 ("Lupin's March 19, 2025 Paragraph IV Notice Letter"), Defendant Lupin Limited stated that Lupin's ANDA contained a certification, pursuant to 21 U.S.C. § 355(j)(2)(A)(vii)(IV), that no valid claim of the '083 patent will be infringed by the manufacture, importation, use, or sale of Lupin's ANDA Products (the "March 19, 2025 Paragraph IV Certification"). Defendant Lupin Limited attached an exhibit to its March 19, 2025 letter, in which it purported to allege the factual and legal bases for its March 19, 2025 Paragraph IV Certification.

**ANSWER:** Defendants admit that Lupin Ltd. transmitted a letter dated March 19, 2025 ("Fourth Notice Letter") to Plaintiff, notifying Plaintiff that Lupin Ltd., as the sole applicant, amended ANDA No. 217431 to include a Paragraph IV Certification with respect to the '083 patent. Defendants further admit that Lupin Ltd.'s Fourth Notice Letter included a detailed statement of the factual and legal bases upon which Lupin Ltd. based its Paragraph IV Certification with respect to the '083 patent. Defendants deny all other allegations in paragraph 20.

21. Upon information and belief, if the FDA approves Lupin's ANDA, Defendants will manufacture, distribute, import, offer for sale and/or sell Lupin's ANDA Products throughout the United States, including within the State of Delaware.

**ANSWER:** Defendants admit that Lupin Ltd. submitted ANDA No. 217431 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor granules described in ANDA No. 217431. Defendants deny all other allegations in paragraph 21.

22. This action is being filed within 45 days of Vertex's receipt of Lupin's March 19, 2025 Paragraph IV Notice Letter.

**ANSWER:** The allegations in paragraph 22 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Plaintiff commenced this

action by filing its Complaint on April 11, 2025. Defendants deny all other allegations in paragraph 22.

**JURISDICTION AND VENUE**

23. This case arises under the patent laws of the United States, 35 U.S.C. § 100, *et seq.*, and this Court has jurisdiction over its subject matter under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

**ANSWER:** The allegations in paragraph 23 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that the Complaint purports to state a claim for patent infringement under the patent laws of the United States, Title 35 of the United States Code. Defendants state that Defendants do not contest subject matter jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants deny all other allegations in paragraph 23.

24. This Court has personal jurisdiction over Defendant Lupin Limited because of its regular transaction and/or solicitation of business in this State. Furthermore, by continuously placing its products into the stream of commerce for distribution and consumption in Delaware, and throughout the United States, Defendant Lupin Limited has engaged in the regular conduct of business within this judicial district.

**ANSWER:** The allegations in paragraph 24 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Ltd. manufactures pharmaceutical products, including generic pharmaceutical products. Defendants state that Lupin Ltd. does not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Lupin Ltd. in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants deny all other allegations in paragraph 24.

25. In addition, this Court has personal jurisdiction over Defendant Lupin Limited by virtue of, *inter alia*, its systematic and continuous contacts with the State of Delaware. Upon information and belief, Defendant Lupin Pharmaceuticals, Inc., a wholly owned subsidiary of Lupin Limited, is incorporated in Delaware.

**ANSWER:** The allegations in paragraph 25 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Pharmaceuticals is a corporation organized and existing under the laws of Delaware. Defendants state that Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 25.

26. Defendant Lupin Limited filed ANDA No. 217431 seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of Lupin's ANDA Products in the United States, including in Delaware. Upon information and belief, upon approval of ANDA No. 217431, Defendant Lupin Limited will market, distribute, offer for sale, and/or sell Lupin's ANDA Products in the United States, including in Delaware.

**ANSWER:** The allegations in paragraph 26 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Ltd. submitted ANDA No. 217431 to the FDA under 21 U.S.C. § 355(j), seeking FDA approval of the ivacaftor granules described in ANDA No. 217431. Defendants deny all other allegations in paragraph 26.

27. This Court has personal jurisdiction over Defendant Lupin Pharmaceuticals, Inc. because, among other things, it is a corporation formed under the laws of the state of Delaware and has appointed a registered agent in Delaware to accept service of process. Defendant Lupin Pharmaceuticals, Inc. has therefore purposely availed itself of the benefits and protections of Delaware's laws such that it should reasonably anticipate being haled into court here.

**ANSWER:** The allegations in paragraph 27 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Pharmaceuticals is a corporation organized and existing under the laws of Delaware. Defendants further admit that Lupin Pharmaceuticals has appointed a registered agent in Delaware. Defendants state that Lupin Pharmaceuticals does not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Lupin Pharmaceuticals in this case and solely as they apply to the

proposed products described in ANDA No. 217431. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 27.

28. Upon information and belief, Defendant Lupin Pharmaceuticals, Inc., acting as the agent of Defendant Lupin Limited, markets, distributes, offers for sale, and/or sells in Delaware and elsewhere in the United States generic pharmaceutical products that are manufactured by Defendant Lupin Limited or for which Defendant Lupin Limited is the named applicant on approved ANDAs. Upon information and belief, upon approval of ANDA No. 217431, Defendant Lupin Pharmaceuticals, Inc. will market, distribute, offer for sale, and/or sell Lupin's ANDA Products in the United States, including in Delaware.

**ANSWER:** The allegations in paragraph 28 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Ltd. manufactures pharmaceutical products, including generic pharmaceutical products. Defendants further admit that Lupin Pharmaceuticals distributes pharmaceutical products, including generic pharmaceutical products, in the United States. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 28.

29. Upon information and belief, Defendants have previously consented to suit in this judicial district and have not challenged personal jurisdiction. Defendants have further availed themselves of the jurisdiction of this Court by previously asserting counterclaims in this jurisdiction. *See, e.g.*, *Harmony Biosciences Mgmt., Inc. v. Lupin Ltd. and Lupin Pharmaceuticals, Inc.*, C.A. 25-102-JLH (D.I. 17); *Neurocrine Biosciences, Inc. v. Lupin Ltd. et al.*, C.A. No. 22-0639 (D.I. 6); *Gilead Scis., Inc. v. Lupin Ltd. et al.*, C.A. No. 22-0615 (D.I. 17); *Exeltis USA, Inc. et al. v. Lupin Ltd. et al.*, C.A. No. 22-434 (D.I. 22); *Bayer Pharma AG, et al., v. Lupin Ltd. and Lupin Pharmaceuticals, Inc.*, C.A. No. 21-314-RGA (D.I. 14); *Genentech, Inc., et al. v. Lupin Ltd. and Lupin Pharmaceuticals, Inc.*, C.A. No. 19-109-RGA (D.I. 10); *Bayer Intellectual Property GmbH, et al., v. Lupin Ltd. and Lupin Pharmaceuticals, Inc.*, C.A. No. 17-1047-RGA (D.I. 9).

**ANSWER:** The allegations in paragraph 29 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants state that Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants deny all other allegations in paragraph 29.

30. Additionally, Defendants have not contested personal jurisdiction in this judicial district in its answers to the complaints in the related consolidated action. *See Vertex*

*Pharmaceuticals Incorporated v. Lupin Limited and Lupin Pharmaceuticals, Inc.*, C.A. No. 1:22-cv-00966-RGA (D. Del.), D.I. 12, D.I. 44, D.I. 67.

**ANSWER:** The allegations in paragraph 30 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants state that Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants admit that in *Vertex Pharmaceuticals Incorporated v. Lupin Limited and Lupin Pharmaceuticals, Inc.*, C.A. No. 1:22-cv-00966-RGA (D. Del.), D.I. 12, D.I. 44, and D.I. 67, Defendants stated that "Defendants do not contest personal jurisdiction in this Court solely for purposes of Plaintiff's claims against Defendants in this case and solely as they apply to the proposed product[s] described in ANDA No. 217431." Defendants deny all other allegations in paragraph 30.

31. Venue is proper in this Court for Defendant Lupin Limited under 28 U.S.C. § 1391(c)(3) because Lupin Limited, on information and belief, is not a resident of the United States and may thus be sued in any judicial district.

**ANSWER:** The allegations in paragraph 31 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Ltd. is a company organized and existing under the laws of India. Defendants state that Lupin Ltd. does not contest venue in this Court solely for purposes of Plaintiff's claims against Lupin Ltd. in this case and solely as they apply to the proposed products described in ANDA No. 217431. Defendants deny all other allegations in paragraph 31.

32. Venue is proper in this Court for Defendant Lupin Pharmaceuticals, Inc. under 28 U.S.C. § 1400(b) because, *inter alia*, Lupin Pharmaceuticals, Inc. is a corporation organized and existing under the laws of the State of Delaware.

**ANSWER:** The allegations in paragraph 32 are legal conclusions to which no answer is required. To the extent an answer is required, Defendants admit that Lupin Pharmaceuticals is a

corporation organized and existing under the laws of Delaware. Defendants state that Lupin Pharmaceuticals does not contest venue in this Court solely for purposes of Plaintiff's claims against Lupin Pharmaceuticals in this case and solely as they apply to the proposed products described in ANDA No. 217413. Defendants deny that Lupin Pharmaceuticals is a proper party to this action. Defendants deny all other allegations in paragraph 32.

**CLAIM FOR RELIEF**
**INFRINGEMENT OF U.S. PATENT NO. 12,214,083**

33. Vertex hereby realleges and incorporates by reference the allegations of paragraphs 1 to 32 of this Complaint.

**ANSWER:** Defendants restate and reallege their answers to each of the preceding paragraphs 1-32, as if fully set forth herein.

34. Defendants have infringed one or more claims of the '083 patent, pursuant to 35 U.S.C. § 271(e)(2)(A), by submitting to the FDA and maintaining Lupin's ANDA, by which Defendants seek approval from the FDA to sell, offer to sell, use, and/or engage in the commercial manufacture of Lupin's ANDA Products prior to the expiration of the '083 patent.

**ANSWER:** Denied.

35. Defendants' commercial manufacture, sale, offer for sale, or use of Lupin's ANDA Products within the United States, or importation of Lupin's ANDA Products into the United States, during the term of the '083 patent would infringe, induce the infringement, and/or contribute to the infringement of one or more claims of the '083 patent under 35 U.S.C. §§ 271(a), (b), and/or (c).

**ANSWER:** Denied.

36. Upon information and belief, Defendants have acted with full knowledge of the '083 patent and without a reasonable basis for believing that they would not be liable for infringement of the '083 patent. Notwithstanding this knowledge, Defendants have continued to assert their intent to engage in the commercial manufacture, use, offer for sale, sale, marketing, distribution and/or importation of Lupin's ANDA Products with its proposed labeling immediately and imminently upon approval of Lupin's ANDA. Upon information and belief, through such activities, Defendants specifically intend infringement of the '083 patent.

**ANSWER:** Denied.

37. Upon information and belief, if the FDA approves Lupin's ANDA, Defendants plan and intend to, and will, infringe, actively induce infringement of, and/or contribute to the infringement of the'083 patent, and will do so immediately and imminently upon approval.

**ANSWER:** Denied.

38. Upon information and belief, Defendants know that Lupin's ANDA Products are especially made or adapted for use in infringing the '083 patent, and that Lupin's ANDA Products are not suitable for any substantial non-infringing use. Upon information and belief, Defendants plan and intend to, and will, contribute to infringement of the '083 patent immediately and imminently upon approval of Lupin's ANDA.

**ANSWER:** Denied.

39. Vertex will be harmed substantially and irreparably if Defendants are not enjoined from infringing the '083 patent.

**ANSWER:** Denied.

40. Vertex has no adequate remedy at law.

**ANSWER:** Denied.

41. Vertex is entitled to a permanent injunction against further infringement under 35 U.S.C. § 283.

**ANSWER:** Denied.

42. Vertex is entitled to a finding that this case is exceptional and to an award of attorneys' fees under 35 U.S.C. § 285.

**ANSWER:** Denied.

## PRAYER FOR RELIEF

Defendants deny all remaining allegations not specifically admitted herein. Defendants further deny that Plaintiff is entitled to any judgment or relief requested in the Complaint, or to any relief whatsoever. Defendants respectfully request that the Court: (a) dismiss the Complaint with prejudice; (b) enter judgment in favor of Defendants; (c) award Defendants the reasonable attorneys' fees and costs of defending this action pursuant to 35 U.S.C. § 285; and (d) award Defendants such further relief as the Court deems just and appropriate.

## AFFIRMATIVE DEFENSES

Without prejudice to the denials set forth in their Answer and without admitting any allegations of the Complaint not otherwise admitted, Defendants aver and assert the following Affirmative Defenses to Plaintiff's Complaint.

### FIRST AFFIRMATIVE DEFENSE
### (Noninfringement of U.S. Patent No. 12,214,083)

Plaintiff will not and cannot meet the burden of proof required to show that the manufacture, use, sale, or offer to sell within, and/or importation into, the United States of the proposed ivacaftor granules described in ANDA No. 217431 will directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid and/or enforceable claim of the '083 patent.

### SECOND AFFIRMATIVE DEFENSE
### (Invalidity of U.S. Patent No. 12,214,083)

Upon information and belief, the claims of the '083 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112 and/or the judicial doctrine of obviousness-type double patenting.

## RESERVATION OF DEFENSES

Defendants expressly reserve the right to supplement and/or amend their Answer to Plaintiff's Complaint, including, but not limited to, supplementation and/or amendment of their defenses and amplifications of denials, as additional facts and information become known throughout the course of this case and discovery and hereby reserve any and all defenses.

## COUNTERCLAIMS

Lupin Limited ("Lupin Ltd." or "Counterclaimant"), by its attorneys, alleges the following counterclaims against Vertex Pharmaceuticals Inc. ("Vertex" or "Counterclaim Defendant").

## THE PARTIES

1. Counterclaimant Lupin Ltd. is a corporation organized and existing under the laws of India, with its principal place of business at 3rd Floor, Kalpataru Inspire, Off Western Expressway Highway, Santacruz (East), Mumbai 400 055, India.

2. Upon information and belief, Counterclaim Defendant Vertex is a corporation organized and existing under the laws of Massachusetts with its principal place of business at 50 Northern Avenue, Boston, MA 02210.

**JURISDICTION AND VENUE**

3. This Court has jurisdiction over the subject matter of these counterclaims under 28 U.S.C. §§ 1331, 1338(a), 2201 and 2202, 35 U.S.C. § 1 et seq., and 35 U.S.C. § 271(e)(5).

4. This Court has personal jurisdiction over Counterclaim Defendant because Counterclaim Defendant commenced and continues to maintain this action against Counterclaimant in this district.

5. Venue is proper in this judicial district under 28 U.S.C. §§ 1391(b) and (c), 21 U.S.C. § 355(j)(5)(C)(i)(II), and because Counterclaim Defendant commenced and continues to maintain this action against Counterclaimant in this district.

**REGULATORY FRAMEWORK**

6. Under the Federal Food, Drug, and Cosmetic Act ("FDCA"), 21 U.S.C. §§ 301 et seq., as amended by the Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271) (the "Hatch-Waxman Act"), and the Medicare Prescription Drug, Improvement, and Modernization Act, Pub. L. No. 108-173, 117 Stat. 2066 (2003) (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271), a pharmaceutical company seeking approval from the U.S. Food and Drug Administration ("FDA") to sell a new drug must file a New Drug Application ("NDA"), which

includes specific data concerning the safety and effectiveness of the drug referenced in the NDA, i.e., the reference listed drug ("RLD").

7. The Hatch-Waxman Act provides that NDA holders shall submit to FDA the patent number and expiration date of any patent that the NDA holder believes "claims the drug for which the applicant submitted the [NDA]" and "for which a claim of patent infringement could reasonably be asserted if a person not licensed by the [NDA] owner engaged in the manufacture, use, or sale of the drug." 21 U.S.C. § 355(b)(1). The FDA lists the patent number(s) and expiration date(s) in its publication titled Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book").

8. The Hatch-Waxman Act codified a process for the approval of generic drugs by allowing a generic applicant to seek approval by filing an Abbreviated New Drug Application ("ANDA"). *See* 21 U.S.C. § 355(j).

9. An ANDA must contain a certification with respect to any patent or patents listed in the Orange Book in connection with the RLD. *See id.* at § 355(j)(2)(A)(vii). ANDA filers may make one of four certifications with respect to each listed patent. Pertinent here is the so-called Paragraph IV certification, which asserts that the listed patent is invalid or will not be infringed by the proposed generic drug product. *See id.* at § 355(j)(2)(A)(vii)(IV)("Paragraph IV certification").

**ORANGE BOOK-LISTED PATENTS FOR KALYDECO®**

10. Upon information and belief, Counterclaim Defendant is the holder of NDA No. 207925 on KALYDECO® (ivacaftor) granules, 25 mg/packet, 50 mg/packet, and 75 mg/packet.

11. Upon information and belief, on February 4, 2025, U.S. Patent No. 12,214,083 ("the '083 patent"), titled "Pharmaceutical Composition and Administrations Thereof"—a copy of which Counterclaim Defendant purported to attach to its Complaint as Exhibit A—was issued to

Vertex Pharmaceuticals Incorporated as Assignee. The FDA's Orange Book lists the expiration date of the '083 patent as February 27, 2033.

12. Upon information and belief, Counterclaim Defendant submitted the '083 patent on February 21, 2025 to the FDA for listing in the FDA's Orange Book.

13. Upon information and belief, the '083 patent is owned by Counterclaim Defendant.

**'083 PATENT**

14. The sole independent claim of the '083 patent, claim 1, requires, *inter alia*, a pharmaceutical composition comprising:

(a) a solid dispersion in an amount from about 30 to about 40 percent by weight of the composition, wherein the solid dispersion comprises:

(i) about 80 wt % of amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion,

(ii) about 19.5 wt % of hydroxypropylmethylcellulose acetate succinate (HPMCAS) by weight of the dispersion, and

(iii) about 0.5 wt % sodium lauryl sulfate (SLS) by weight of the dispersion;

(b) mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition, wherein mannitol and lactose are present in a ratio of about 1:3 mannitol to lactose,;

(c) sucralose in an amount from about 0.1 to about 5 percent by weight of the composition;

(d) croscarmellose sodium in an amount from about 1.5 to about 8 percent by weight of the composition;

(e) colloidal silicon dioxide in an amount from about 0.1 to about 5 percent by weight of the composition; and

(f) magnesium stearate in an amount from about 0.1 to about 7 percent by weight of the composition;

(*See* Exhibit A, '083 patent at col. 190 ln. 58 – col. 191 ln. 14)

15. The '083 patent issued from U.S. Patent Application No. 18/355,475 ("the '475 application") filed on July 20, 2023 and is a continuation of U.S. Patent Application No. 17/475,622 filed on September 15, 2021, now U.S. Patent No. 11,752,106 ("the '106 patent"), which is a continuation of U.S. Patent Application No. 16/299,675 filed on March 12, 2019, now U.S. Patent No. 11,147,770 ("the '770 patent"), which is a continuation of U.S. Patent Application No. 15/181,114 ("the '114 application") filed on June 13, 2016, now U.S. Patent No. 10,272,046 ("the '046 patent"), which is a continuation of U.S. Patent Application No. 14/715,682 filed on May 19, 2015, which is a continuation of U.S. Patent Application No. 14/510,507, filed on October 9, 2014, which is a continuation of U.S. Patent Application No. 14/286,856, filed on May 23, 2014, now U.S. Patent No. 8,883,206 ("the '206 patent"), which is a continuation of U.S. Patent Application No. 13/779,654, filed on February 27, 2013. (*See* Exhibit A, '083 patent, Related U.S. Application Data at p. 1-2).

16. The '114 application was filed on June 13, 2016 containing 34 claims. (Exhibit 1, '046 patent PH, June 13, 2016 Transmittal of New Appl. at 278-82.) In a Preliminary Amendment filed on December 28, 2016, applicant cancelled claims 1-11, 23, and 28-30. (Exhibit 2, '046 patent PH, Dec. 28, 2016 Preliminary Amendment at 2-4.) Claim 12, the sole remaining independent claim, reads as follows:

12. A pharmaceutical composition comprising:

about 35 wt% of a solid dispersion by weight of the composition, wherein the dispersion comprises about 80 wt% of substantially amorphous or amorphous Compound 1 by weight of the dispersion, about 19.5 wt% of HPMCAS by weight of the dispersion, and about 0.5 wt% SLS by weight of the dispersion;

about 13.5 wt% of mannitol by weight of the composition;

about 41 wt% of lactose by weight of the composition;

about 2 wt% of sucralose by weight of the composition;

about 6 wt% of croscarmellose sodium by weight of the composition;

about 1 wt% of colloidal silicon dioxide by weight of the composition; and

about 1.5 wt% of magnesium stearate by weight of the composition.

(*Id.* at 2.)

17. On January 11, 2017, the Examiner issued a Non-Final Rejection, rejecting claims 12-22, 24-27, and 31-34. (Exhibit 3, '046 patent PH, Jan. 11, 2017 Non-Final Rejection at 1-11.) The Examiner rejected claims 12-22, 24-27, and 31-34, *inter alia*, under 35 U.S.C. § 103(a) as unpatentable over Douku et al. (US Pre-Grant Publication No° 2012/0064157; also published as WO 2012/027731) ("Douku"). (*Id.* at 3). The Examiner stated:

> The reference is considered to teach and suggest the instantly claimed composition. **Douku** discloses in **claim 21**, the composition of claim 1 wherein the solid dispersion of Compound 1 is present in an amount ranging from 35-47 wt% of the composition. Sucralose is present at about 2 wt% of the composition, CMC-Na represents about 3 wt% to about 6 wt% of the composition, silicon dioxide is present at about 1 wt% of the composition and magnesium stearate is present at about 1.5 wt% of the composition. **Claim 21** teaches that mannitol is present from about 42-57 wt% of the composition as filler. The recited mannitol and lactose limitations of [sic] are, however, considered to be taught by **claim 6** which not only teaches the filler as being embodied by more than one filler compound but also that mannitol and lactose are used in concert. As such, the reference is considered to teach and suggest the combined use of mannitol and lactose as the filler components of the composition.

(*Id.* at 4-5 (emphasis in original).)

18. On July 11, 2017, applicant filed an Amendment, amending claims 12 and 13. (Exhibit 4, '046 patent PH, July 11, 2017 Amendment at 2-3, 6.) Applicant amended claim 12 as follows:

> 12. (Currently Amended) A pharmaceutical composition in a unit dose form comprising one or a plurality of granules, pellets, particles or mini-tablets, wherein the composition comprises ~~comprising~~:
>
> ~~about 35% of~~ a solid dispersion in an amount from about 30 to about 50 percent by weight of the com position, wherein the dispersion comprises about 80 wt% of substantially amorphous or amorphous Compound by weight of the dispersion, about 19.5 wt% of HPMCAS by weight of the dispersion, and about 0.5 wt% SLS by weight of the dispersion;
>
> ~~about 13.5 wt% of mannitol by weight of the composition;~~
>
> ~~about 41 wt% of lactose by weight of composition;~~
>
> mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition, wherein mannitol and lactose are present in a ratio of about 1:3 mannitol to lactose;
>
> ~~about 2 wt% of~~ sucralose in an amount from about 1.5 to about 2.5 percent by weight of the composition;
>
> ~~about 6 wt% of~~ croscarmellose sodium in an amount from about 4 to about 8 percent by weight of the composition;
>
> ~~about 1 wt% of~~ colloidal silicon dioxide in an amount from about 0.5 to about 1.5 percent by weight of the composition; and
>
> ~~about 1.5 wt% of~~ magnesium stearate in an amount from about 0.5 to about 1.5 percent by weight of the composition.

(*Id*. at 2.)

19. In the July 11, 2017 amendment, Applicant argued that:

> [A]lthough *Dokou 2012* broadly discloses the use of fillers, every example in *Dokou 2012* incorporates mannitol as the only filler . . . Nothing in *Dokou 2012* claims 6-8 or 21 would guide a person of skill in the art to the choice of mannitol and lactose as a binary filler combination, nor does anything in *Dokou 2012* suggest their inclusion at a ratio of 1:3 by weight. Therefore, contrary to the Examiner's assertions, *Dokou 2012* does not teach or suggest

> any binary filler, and in particular does not teach or suggest a composition comprising a mannitol/lactose filler at the ratio recited in Applicant's claims.

(*Id.* at 7.)

20. On July 19, 2017, the Examiner issued a Final Rejection, again rejecting claims 12-22, 24-27, and 31-34 under 35 U.S.C. § 103(a) as unpatentable over Douku et al. (Exhibit 5, '046 patent PH, July 19, 2017 Final Rejection at 4-9.) The Examiner stated that applicants' arguments were not persuasive. (*Id*. at 9.)

21. On January 12, 2018, applicant filed an Amendment, amending claim 12 "to introduce the full chemical name of Compound 1." (Exhibit 6, '046 patent PH, Jan. 12, 2018 Amendment at 6.) Applicant argued:

> Applicants' initial pediatric granule formulations, which contained mannitol as the sole filler, had several technical problems related to manufacturability and reproducibility . . . . It required months of effort to identify the specific combination and ratio of fillers (lactose and mannitol at a ratio of 1:3) that had the desirable level of compressibility required for reproducible manufacturing.

(*Id.* at 7.)

22. On January 22, 2018, the Examiner issued a Non-Final Rejection, maintaining a rejection of claims 12-22, 24-27, and 31-34 under 35 U.S.C. § 103(a) as unpatentable over Douku et al. (Exhibit 7, '046 patent PH, Jan. 22, 2018 Non-Final Rejection at 3-12.)

23. On July 23, 2018, applicant filed an Amendment, amending claim 12 to include the limitation "wherein the composition does not comprise SLS outside the solid dispersion." (Exhibit 8, '046 patent PH, July 23, 2018 Amendment at 2.) Applicant further argued that "nowhere in Dokou 2012 is a binary mixture of mannitol and lactose taught or suggested." (*Id.* at 10.) Applicant also argued:

> Nothing in Dokou 2012 suggests that a composition having a combination of solid dispersion of Compound 1 in an amount from about 30 to about 50

> percent by weight of the composition; mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition and in a ratio of about 1:3 mannitol to lactose; and croscarmellose sodium in an amount from about 4 to about 8 percent by weight of the composition would have improved bioavailability.

(*Id.* at 11.)

24. On December 12, 2018, the Examiner issued a Notice of Allowance, allowing claims 12-22, 24-27, and 31-34. (Exhibit 9, '046 patent PH, Dec. 12, 2018 Notice of Allowability 1-3.)

25. The '622 application was filed on September 15, 2021 containing 34 claims. (Exhibit 10, '106 patent PH, September 15, 2021 Transmittal of New Appl. at 278-82.)

26. In a Preliminary Amendment filed on April 27, 2022, applicant cancelled claims 1-34 and added new claims 35-54 (Exhibit 11, '106 patent PH, April 27, 2022 Response to Notice to File Missing Parts and Preliminary Amendment at 2-6.) Claim 35, the sole remaining independent claim, reads as follows:

> 35. (New) A pharmaceutical composition in a unit dose form comprising one or a plurality of granules, pellets, particles or mini-tablets, wherein the composition comprises:
>
> (a) a solid dispersion in an amount from 30 to 40 percent by weight of the composition, wherein the solid dispersion comprises:
>
> (i) about 80 wt% of substantially amorphous or amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion,
>
> (ii) about 19.5 wt% of hydroxypropylmethylcellulose acetate succinate (HPMCAS) by weight of the dispersion, and
>
> (iii) about 0.5 wt% sodium lauryl sulfate (SLS) by weight of the dispersion;

(b) a binary filler, wherein the binary filler comprises mannitol and lactose in a ratio of about 1:3 mannitol to lactose;

(c) a sweetener, wherein the sweetener is sucralose;

(d) a disintegrant;

(e) a glidant; and

(f) a lubricant;

wherein the unit dose form comprises at least about 5 mg of substantially amorphous or amorphous Compound 1,

and wherein substantially amorphous Compound 1 has less than 15% crystallinity.

(*Id*. at 2-3.)

27. On December 12, 2022, the Examiner issued a Non-Final Rejection, rejecting claims 35-54. (Exhibit 12, '106 patent PH, December 12, 2022 Non-Final Rejection at 1-11.) The Examiner rejected claims 35-54 as unpatentable on the grounds of nonstatutory double patenting over claims 1-10 of the '206 patent, claims 1-23 of the '046 patent, claims 1-22 of the '770 patent, and claims 1, 3, 4, 6, 7, 10-13, 18, 20, 21, and 23-25 of U.S. Patent No. 10,646,481 ("the '481 patent"). (*Id.* at 4-12.)

28. On April 12, 2023, applicant filed a Reply to Office Action, Declaration under 37 C.F.R. § 1.132, and terminal disclaimers with regards to the '206 patent, '046 patent, and '770 patent. In the Reply to Office Action, the applicant traversed the double patenting rejection over the '481 patent, arguing that:

> Claims 35-54 recite pharmaceutical compositions comprising Compound 1 and a binary filler of mannitol and lactose in a ratio of about 1:3, and methods of treatment using the pharmaceutical compositions. U.S. Patent No. 11,147,770 ("the '770 patent"), the parent of this application, granted with claims reciting pharmaceutical compositions with these features. The claims of the '770 patent were found to be patentable over U.S. Publication No. 2010/0256184 Al ("Rowe.").

*Rowe* and the ’481 patent each claim the benefit of priority of U.S. Patent Application No. 12/583,066. *Rowe* is a continuation-in-part of U.S. Patent Application No. 12/583,066, while the ’481 patent is a continuation of U.S. Patent Application No. 14/135,323, which is a continuation of U.S. Patent Application No. 12/583,066. *Rowe* and the ’481 patent share substantially similar disclosures. Thus, pending claims 35-54 are patentably distinct from the claims of the ’481 patent for at least the same reasons that the claims of the ’770 patent are patentable over the disclosure of *Rowe*.

In the Notice of Allowance for the ’770 patent, the Examiner states that *Rowe* “does not provide the motivation to the skilled artisan to arrive at the instantly claimed ratio” of 1:3 mannitol to lactose. Thus, as the Examiner has previously acknowledged, at least the feature of a binary filler comprising 1:3 mannitol to lactose is nonobvious in view of the prior art. This feature was not taught or suggested by the disclosure of the ’481 patent, let alone its granted claims.

* * *

As Applicant explained during prosecution of the '770 patent, *Rowe* does not teach a pharmaceutical composition comprising Compound 1 suitable for administration to younger children that retains the bioavailability profile of the adult formulation. . . . The claimed compositions also differ from *Rowe, inter alia*, because they comprise a binary filler of mannitol and lactose in a 1:3 ratio and sucralose as a sweetener.

*Rowe* refers to a genus of “suitable” fillers for use in its pharmaceutical tablet formulations comprising Compound 1 - but exemplifies only the use of lactose as a single component filler. *Rowe* does not specifically suggest a binary filler or specify any particular combination of fillers for use in pharmaceutical compositions comprising Compound 1. *Rowe* discloses a preference for use of a single filler composition and does not provide any rationale for choosing a combination of fillers over a single filler composition. Nor does *Rowe* suggest that there would be any problem with using one filler over another filler in pharmaceutical compositions comprising Compound 1.

* * *

During prosecution of the '770 patent, Applicant submitted the Declaration of Dr. Hayden Thomas ("Declaration") to support the patentability of pharmaceutical compositions with the features recited in claim 35 over the prior art. The Declaration is submitted as an attachment to this paper.

As Dr. Thomas states, the selection of fillers in the pediatric formulation of Compound 1 had a significant impact not only on the development of a formulation that was sufficiently palatable to mask the bitter and lingering

> taste of Compound 1, but also on the ability to overcome unexpected challenges with processability, compressibility, and content uniformity. Declaration at ¶¶ 6-11. The existence of these challenges was not suggested by or obvious from *Rowe*. . . . A formulation containing mannitol as the single filler resulted in granules that exhibited significantly reduced bioavailability (as compared to the commercial adult tablet of *Rowe*) as well as problems associated with high ejection forces required to remove granules from the die after compression. Declaration at ¶¶ 8-10.
>
> Nothing in *Rowe* suggests that problems with palatability and manufacturability of mini-tablets comprising ivacaftor could be overcome by selecting a binary filler composed of 1:3 mannitol to lactose. Declaration at ¶ 11. Accordingly, the teachings of Rowe do not render Applicant's claims obvious.
>
> * * *
>
> The claims of the ’481 patent share at least the deficiencies of *Rowe* explained above. Thus, the pending claims are patentably distinct from the claims of the ’481 patent for similar reasons. Applicant traverses the double patenting rejection and respectfully requests that the double patenting rejection over the ’481 patent be withdrawn.

(Exhibit 13, ’106 patent PH, April 12, 2023 Reply at 7-12.)

29. On April 21, 2023, the Examiner issued a Notice of Allowance, allowing claims 35-54. (Exhibit 14, ’106 patent PH, April 21, 2023 Notice of Allowance 1-5.) In the Notice of Allowance, the Examiner stated:

> Applicants’ remarks and Rule 132 Declaration have been carefully considered in response to the remaining Nonstatutory Double Patenting rejection raised over Rowe et al. (USPN 10,646,481 B2)
>
> Of particular interest within the totality of the response was Mr. Hayden’s filed affidavit discussing evidence of criticality for the claimed 1:3 ratio of mannitol to lactose in the binary filler of the composition. Specifically, ¶¶ 10-11 of the declaration submitted evidence not previously found in the entirety of the prosecution history discussing Applicant’s discovered advantages for reciting the above ratio.
>
> * * *
>
> Applicants attest that their research revealed this [1:3 mannitol to lactose] [] blend to not only provide an aesthetically pleasing masking for the bitter tasting drug, but more critically, it provided a low enough ejection force to be able to remove the completed dosage forms from their dies without

> damaging the dosage form itself. This critical feature allowed the dosage forms to be repeatedly produced with the quality and validation aspects (i.e., lack of damage, content uniformity, etc.) required to consistently deliver the same dose of ivacaftor from each tablet.
>
> Those dosage blends tested that employed higher quantities of mannitol in the ratio (i.e., 1:1 and 3:1) were reported as requiring far greater force to eject them from the die which summarily resulted in damage to enough of the tablets to warrant the higher ratios as being undesirable.
>
> This evidence, on its own, is persuasive in overcoming the teachings of Rowe, alone or in combination with the secondary teachings.
>
> The Examiner maintains that Rowe does teach and suggest: (1) the combination of mannitol with lactose as the filler component, (2) total amounts of the filler that may be used in the overall composition, and (3) amounts of lactose within the totality of the filler component. Ultimately, Rowe is considered to provide teachings that encompass the recited filler and ratio. However, in view of the newly filed evidence, Rowe does not provide the motivation to the skilled artisan to arrive at the instantly claimed ratio.
>
> In view of Mr. Hayden's submission, the Examiner withdraws the rejection.

(*Id.* at 2-4.)

30. The ’475 application was filed on July 20, 2023 containing 34 claims. (Exhibit 15, ’083 patent PH, July 20, 2023 Transmittal of New Appl. at 278-82.)

31. In a Preliminary Amendment filed on February 5, 2024, applicant cancelled claims 1-34 and added new claims 35-54 (Exhibit 16, ’083 patent PH, February 5, 2024 Response to Notice to File Missing Parts and Preliminary Amendment at 2-4.) Claim 35, the sole remaining independent claim, reads as follows:

35. (New) A pharmaceutical composition in a unit dose form comprising a plurality of granules or mini-tablets, wherein the composition comprises:

a) a solid dispersion in an amount from about 30 to about 40 percent by weight of the composition, wherein the dispersion comprises:
   i. about 80 wt% of amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion,
   ii. about 19.5 wt% of HPMCAS by weight of the dispersion, and
   iii. about 0.5 wt% SLS by weight of the dispersion;

b) mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition, wherein mannitol and lactose are present in a ratio of about 1:3 mannitol to lactose;
c) sucralose in an amount from about 0.1 to about 5 percent by weight of the composition;
d) croscarmellose sodium in an amount from about 1.5 to about 8 percent by weight of the composition;
e) colloidal silicon dioxide in an amount from about 0.1 to about 5 percent by weight of the composition; and
f) magnesium stearate in an amount from about 0.1 to about 7 percent by weight of the composition;

wherein the unit dose form comprises at least about 5 mg of amorphous Compound 1, and wherein less than about 15 wt% of the Compound 1 is crystalline.

(*Id.* at 2.)

32. On March 22, 2024, the Examiner issued a Non-Final Rejection, rejecting claims 35-54. (Exhibit 17, '083 patent PH, March 22, 2024 Non-Final Rejection at 1-15.) The Examiner rejected claims 35-54 as unpatentable on the grounds of nonstatutory double patenting over claims 1-10 of the '206 patent, claims 1-23 of the '046 patent, claims 1-22 of the '770 patent, and claims 1, 3, 4, 6, 7, 10-13, 18, 20, 21, and 23-25 of the '481 patent. (*Id.* at 4-12.) The Examiner rejected claims 35-48 and 51-54 as unpatentable on the grounds of nonstatutory double patenting over claims 1-20 of the '106 patent. (*Id.* at 13-14.)

33. On September 19, 2024, applicant filed an Amendment and Reply to Office Action and terminal disclaimers with regards to the '206 patent, '046 patent, '770 patent, and '106 patent.

(Exhibit 18, '083 patent PH, September 19, 2024 Reply at 1-10.) In the Reply to Office Action, the applicant traversed the double patenting rejection over the '481 patent, arguing that:

> Applicant respectfully disagrees and traverses the double patenting rejection over the '481 patent at least because, in spite of an initial obviousness rejection over the '481 patent, the Examiner allowed parent patent U.S. Patent C No. 11,752,106 ("the 106 patent").
>
> The primary difference between claim 1 of the '106 patent and Applicant's amended claim 35 is that Applicant's amended claim 35 recites specific excipients and wt% ranges for the excipients. For ease of reference, the relevant claims are summarized in the following table:

| U.S. Patent No. 11,752,106 (Issued claim 1) | U.S. Patent No. 18/355,475 (Amended claim 35) |
|---|---|
| 1. A pharmaceutical composition in a unit dose form comprising one or a plurality of granules, pellets, particles or mini-tablets, wherein the composition comprises: | 35. A pharmaceutical composition in a unit dose form comprising a plurality of granules or mini-tablets, wherein the composition comprises: |
| (a) a solid dispersion in an amount from 30 to 40 percent by weight of the composition, wherein the solid dispersion comprises: | a) a solid dispersion in an amount from about 30 to about 40 percent by weight of the composition, wherein the dispersion comprises: |
| (i) about 80 wt % of substantially amorphous or amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion, | i. about 80 wt% of amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion, |
| (ii) about 19.5 wt % of hydroxypropylmethylcellulose acetate succinate (HPMCAS) by weight of the dispersion, and | ii. about 19.5 wt% of hydroxypropylmethylcellulose acetate succinate (HPMCAS) by weight of the dispersion, and |
| (iii) about 0.5 wt % sodium lauryl sulfate (SLS) by weight of the dispersion; | iii. about 0.5 wt% of sodium lauryl sulfate (SLS) by weight of the dispersion; |
| (b) a binary filler, wherein the binary filler comprises mannitol and lactose in a ratio of about 1:3 mannitol to lactose; | b) mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition, wherein mannitol and lactose are present in a ratio of about 1:3 mannitol to lactose; |
| (c) a sweetener, wherein the sweetener is sucralose; | c) sucralose in an amount from about 0.1 to about 5 percent by weight of the composition; |
| (d) a disintegrant; | d) croscarmellose sodium in an amount from about 1.5 to about 8 percent by weight of the composition; |
| (e) a glidant; and | e) colloidal silicon dioxide in an amount from about 0.1 to about 5 percent by weight of the composition; and |
| (f) a lubricant; | f) magnesium stearate in an amount from about 0.1 to about 7 percent by weight of the composition; |
| wherein the unit dose form comprises at least about 5 mg of substantially amorphous or amorphous Compound 1, and | wherein the unit dose form comprises at least about 5 mg of amorphous Compound 1, and |
| wherein substantially amorphous Compound 1 has less than 15% crystallinity. | wherein less than about 15 wt% of the Compound 1 is crystalline. |

> The Examiner acknowledged the non-obviousness of claim 1 of the ’106 patent over a citation of the '481 patent, at least because claim 1 of the ’106 patent (like claim 35 of Applicant's pending claims) recites a binary filler of about 1:3 mannitol and lactose, which Applicant demonstrated was responsible for unexpected properties that include improved palatability, manufacturability, and bioavailability. In the Notice of Allowance for the ’106 patent (“Notice of Allowance”) mailed on April 21, 2023, the Examiner acknowledged the unexpected properties brought about by the binary filler in the statement of reasons for allowance:
>
> > Applicants' remarks and Rule 132 Declaration have been carefully considered in response to the remaining Nonstatutory Double Patenting rejection raised over Rowe et al. (USPN 10,646,481 B2).... This evidence, on its own, is persuasive in overcoming the teachings of Rowe, alone or in combination with the secondary teachings. The Examiner maintains that Rowe does teach and suggest: (1) the combination of mannitol with lactose as the filler component, (2) total amounts of the filler that may be used in the overall composition, and (3) amounts of lactose within the totality of the filler component. Ultimately, Rowe is considered to provide teachings that encompass the recited filler and ratio. However, in view of the newly filed evidence, **Rowe does not provide the motivation to the skilled artisan to arrive at the instantly claimed ratio**. In view of Mr. Hayden's submission, the Examiner **withdraws** the rejection.
>
> Notice of Allowance at 2 and 4 (emphasis added).
>
> Applicant's amended claims are directed to pharmaceutical compositions comprising Compound 1 and a binary filler of about 1:3 mannitol and lactose as recited in claim 1 of the ’106 patent. In other words, Applicant's pending claims share the same patentable feature of claim 1 of the ’106 patent. Therefore, the amended claims are patentably distinct from the ’481 patent for at least the same reasons that claim 1 of the '106 patent is patentably distinct from the '481 patent. Accordingly, Applicant respectfully requests that the nonstatutory double patenting rejection in view of U.S. Patent No. 10,646,481 be withdrawn.

(*Id.* at 7-9.)

34. On September 27, 2024, the Examiner issued a Notice of Allowance, allowing claims 35-54. (Exhibit 19, ’083 patent PH, September 27, 2024 Notice of Allowance 1-4.) In the Notice of Allowance, the Examiner stated:

> Applicants' remarks traversing the nonstatutory double patenting rejection over USPN 10,646,481 are acknowledged. Review of the Notice of Allowance in the parent application reveals that this rejection was withdrawn in view of the evidence presented therein. Said rejection is hereby withdrawn.

(*Id.* at 2-3.)

**LUPIN'S ANDA**

35. In April 2022, Lupin Ltd. filed ANDA No. 217431 with the FDA seeking FDA approval to engage in the commercial manufacture, use or sale of ivacaftor granules, 25 mg, 50 mg and 75 mg ("Proposed ANDA Products").

36. Because Lupin Ltd. seeks FDA approval to engage in the commercial manufacture, use or sale of Lupin Ltd.'s Proposed ANDA Products before expiration of the '083 patent, Lupin Ltd.'s ANDA was amended on March 19, 2025 to include a Paragraph IV certification to that patent.

37. Lupin Ltd. transmitted a letter dated June 9, 2022 to Counterclaim Defendant, notifying Counterclaim Defendant that ANDA No. 217431 had been submitted to the FDA under 21 U.S.C. § 355(j), which included Paragraph IV certifications that no valid claim of the '206, '481, and the '046 patents would be infringed by the proposed ivacaftor granules, 25 mg, 50 mg and 75 mg that are the subject of ANDA No. 217431 ("First Notice Letter"). In its First Notice Letter, Lupin Ltd. included a detailed statement of the factual and legal bases upon which it based its Paragraph IV certifications and extended to Counterclaim Defendant an Offer of Confidential Access to Lupin Ltd.'s ANDA No. 217431.

38. Lupin Ltd.'s First Notice Letter included the factual and legal basis on which Vertex is estopped from asserting infringement of claim 1 of the '046 patent—the sole independent claim—due to the doctrine of prosecution history estoppel.

39. On July 22, 2022, Counterclaim Defendant filed a patent infringement lawsuit against Lupin Ltd., alleging that Lupin Ltd.'s Proposed ANDA Products would infringe the '206, '046, '481, and '770 patents.

40. On December 16, 2022, Counterclaimant produced Lupin Ltd.'s ANDA to Counterclaim Defendant.

41. Counterclaim Defendant has been on notice since December 16, 2022, that Lupin's Proposed ANDA Products, as described in Lupin Ltd.'s ANDA, do not meet the limitations of the '206, '046, '481, and '770 patents.

42. Lupin Ltd. transmitted a letter dated March 19, 2025 ("Fourth Notice Letter") to Counterclaim Defendant, notifying Counterclaim Defendant that ANDA No. 217431 had been submitted to the FDA under 21 U.S.C. § 355(j), and was amended to include a Paragraph IV certification that no valid claim of the '083 patent would be infringed by the proposed granules, 25 mg, 50 mg and 75 mg that are the subject of ANDA No. 217431. In its Fourth Notice Letter, Lupin Ltd. included a detailed statement of the factual and legal bases upon which it based its Paragraph IV certification and extended to Counterclaim Defendant an Offer of Confidential Access to Lupin Ltd.'s ANDA No. 217431.

43. Lupin Ltd.'s Fourth Notice Letter included the factual and legal basis on which Vertex is estopped from asserting infringement of claim 1 of the '083 patent—the sole independent claim—due to the doctrine of prosecution history estoppel.

44. On April 11, 2025 Counterclaim Defendant filed a patent infringement lawsuit against Lupin Ltd., alleging that Lupin Ltd.'s Proposed ANDA Products would infringe the '083 patent.

45. Counterclaim Defendant has been on notice since before Counterclaim Defendant filed a patent infringement lawsuit against Lupin Ltd. for the '083 patent, that Lupin's Proposed ANDA Products, as described in Lupin Ltd.'s ANDA, do not meet the limitations of the '083 patent.

46. As a consequence of Counterclaim Defendant's Complaint against Lupin Ltd., there is now an existing and continuing actual controversy between Counterclaim Defendant and Lupin Ltd. concerning the alleged infringement and validity of the '083 patent.

47. By listing and maintaining the '083 patent in the Orange Book, Counterclaim Defendant represents that the patent "claims the drug for which the applicant submitted the [KALYDECO®] application" and "for which a claim for patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." See 21 U.S.C. § 355(b)(1).

48. Accordingly, by virtue of listing and maintaining the '083 patent in the Orange Book, Counterclaim Defendant represents that an infringement suit based on the '083 patent could be asserted against Lupin Ltd. because Lupin Ltd. is seeking approval to market its Proposed ANDA Products before the expiration of the '083 patent.

49. Until and unless Lupin Ltd. obtains a court decision of noninfringement and/or invalidity on the '083 patent, Lupin Ltd. potentially faces infringement liability if it commences marketing before the '083 patent expires.

50. Accordingly, there is an actual, substantial and continuing justiciable controversy between Lupin Ltd. and Counterclaim Defendant regarding the '083 patent over which the Court can and should exercise jurisdiction and declare the rights of the parties.

**COUNT I**
**(Declaratory Judgment of Noninfringement of the '083 Patent)**

51. Counterclaimant repeats and reasserts the allegations in paragraphs 1 through 50 above as though fully set forth herein.

52. The proposed ivacaftor granules, 25 mg, 50 mg, and 75 mg, that are the subject of ANDA No. 217431 would not and will not directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the ’083 patent.

53. Vertex is estopped, due to the doctrine of prosecution history estoppel, from asserting infringement of the ’083 patent against a pharmaceutical composition that does not comprise (a) a solid dispersion in an amount from about 30 to about 40 percent by weight of the composition, wherein the dispersion comprises: (i) about 80 wt % of amorphous N-[2,4-bis(1,1-dimethylethyl)-5-hydroxyphenyl]-1,4-dihydro-4-oxoquinoline-3-carboxamide (Compound 1) by weight of the dispersion (ii) about 19.5 wt % of hydroxypropylmethylcellulose acetate succinate (HPMCAS) by weight of the dispersion, and (iii) about 0.5 wt % sodium lauryl sulfate (SLS) by weight of the dispersion; (b) mannitol and lactose in an amount from about 30 to about 60 percent by weight of the composition, wherein mannitol and lactose are present in a ratio of about 1:3 mannitol to lactose; (c) sucralose in an amount from about 0.1 to about 5 percent by weight of the composition; (d) croscarmellose sodium in an amount from about 1.5 to about 8 percent by weight of the composition; (e) colloidal silicon dioxide in an amount from about 0.1 to about 5 percent by weight of the composition; and (f) magnesium stearate in an amount from about 0.1 to about 7 percent by weight of the composition.

54. Vertex is estopped, due to the doctrine of prosecution history estoppel, from asserting that the claims of the ’083 patent encompass the proposed ivacaftor granules, 25 mg, 50 mg, and 75 mg, that are the subject of ANDA No. 217431.

## COUNT II
**(Declaratory Judgment of Invalidity of the ’083 Patent)**

55. Counterclaimant repeats and reasserts the allegations in paragraphs 1 through 54 above as though fully set forth herein.

56. The claims of the ’083 patent are invalid for failure to comply with one or more of the provisions of Title 35 of the United States Code, including, but not limited to, §§ 101, 102, 103, and/or 112 and/or the judicial doctrine of obviousness-type double patenting.

57. For the reasons explained in Lupin Ltd.’s Fourth Notice Letter dated March 19, 2025, transmitted to Counterclaim Defendant, which is incorporated fully by reference herein, the claims of the ’083 patent are invalid at least under 35 U.S.C. §§ 102 and/or 103 and/or the judicial doctrine of obviousness-type double patenting, in view of the prior art cited therein.

58. Counterclaimant reserves the right to provide additional and/or modified bases for invalidity of the ’083 patent in its contentions, responses to discovery requests, expert reports, and/or pleadings filed and/or served later in this action.

**PRAYER FOR RELIEF**

WHEREFORE, Counterclaimant respectfully requests the Court to enter judgment against Counterclaim Defendant Vertex as follows:

A. A declaration that Counterclaimant has not and will not directly or indirectly infringe, either literally or under the doctrine of equivalents, any valid claim of the ’083 patent;

B. A declaration that the claims of the ’083 patent are invalid for failure to comply with one or more of the provisions of 35 U.S.C. §§ 100 et seq., including §§ 101, 102, 103, and/or 112 and/or the judicial doctrine of obviousness-type double patenting;

C. A declaration that Counterclaim Defendant Vertex takes nothing by its Complaint;

D. A dismissal of Counterclaim Defendant Vertex’s Complaint with prejudice;

E. An award to Counterclaimant of its reasonable costs and attorneys’ fees incurred in this action pursuant to 35 U.S.C. § 285; and

F. An award of any other and further relief that this Court may deem just and proper.

DATED: May 2, 2025

By: /s/ *Francis J. Murphy*

MURPHY & LANDON
Francis J. Murphy (#223)
1011 Centre Road, Suite 210
Wilmington, Delaware 19806
(302) 472-8103
(302) 472-8135 (fax)
fmurphy@msllaw.com

*Of Counsel*

Keith D. Parr
James T. Peterka
Nina Vachhani
Amy M. Lange
Jacob C. Britz
BUCHANAN INGERSOLL & ROONEY PC
150 N. Riverside Plaza, Suite 2800
Chicago, IL 60606-1599
(312) 261-8777

*Counsel for Lupin Ltd. and Lupin Pharmaceuticals, Inc.*