



ANDA 217431

ANDA TENTATIVE APPROVAL

Lupin Pharmaceuticals, Inc.
U.S. Agent for Lupin Limited
111 South Calvert Street
Harborplace Tower, 21st Floor
Baltimore, MD 21202
Attention: Debashis Mohanty
Associate Director - Regulatory Affairs

Dear Debashis Mohanty:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on April 13, 2022, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Ivacaftor Oral Granules, 25 mg, 50 mg and 75 mg per unit dose packet.

Reference is also made to the complete response letter issued by this office on February 13, 2024, and to any amendments thereafter.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug meets the requirements for approval under the FD&C Act. We have determined your Ivacaftor Oral Granules, 25 mg, 50 mg and 75 mg per unit dose packet to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Kalydeco Oral Granules, 25 mg, 50 mg and 75 mg, of Vertex Pharmaceuticals Inc. (Vertex) NDA - 207925.

However, we are unable to grant final approval to your ANDA at this time because of the patent/exclusivity issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the Agency at this time (e.g., information in your ANDA and the status of current good manufacturing practices (cGMPs) of the facilities used in the manufacturing and testing of the drug product). This determination is subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the FD&C Act.

The RLD upon which you have based your ANDA, Vertex's Kalydeco Oral Granules, 25 mg, 50 mg and 75 mg, is subject to periods of patent protection. The following patents and expiration dates are currently listed in the Agency's publication titled *Approved Drug Products with Therapeutic Equivalence Evaluations* (the "Orange Book"):

| <u>U.S. Patent Number</u> | <u>Expiration Date</u> |
|------------------------------|------------------------|
| 7,495,103 (the '103 patent) | May 20, 2027 |
| 8,324,242 (the '242 patent) | August 5, 2027 |
| 8,354,427 (the '427 patent) | July 6, 2026 |
| 8,410,274 (the '274 patent) | December 28, 2026 |
| 8,629,162 (the '162 patent) | June 24, 2025 |
| 8,754,224 (the '224 patent) | December 28, 2026 |
| 8,883,206 (the '206 patent) | February 27, 2033 |
| 9,670,163 (the '163 patent) | December 28, 2026 |
| 10,272,046 (the '046 patent) | February 27, 2033 |
| 10,646,481 (the '481 patent) | August 13, 2029 |
| 11,147,770 (the '770 patent) | February 27, 2033 |
| 11,564,916 (the '916 patent) | August 13, 2029 |
| 11,752,106 (the '106 patent) | February 27, 2033 |

With respect to the '103, '242, '427, '274, '162, '224 and '163 patents, your ANDA contains paragraph III certifications to each of the patents under section 505(j)(2)(A)(vii)(III) of the FD&C Act stating that Lupin Limited (Lupin) will not market Ivacaftor Oral Granules, 25 mg, 50 mg and 75 mg per unit dose packet prior to the expiration of the patents. Therefore, final approval of your ANDA may not be granted pursuant to section 505(j)(5)(B)(ii) of the FD&C Act until the '242 patent has expired, currently August 5, 2027.

Your ANDA contains paragraph IV certifications to the '206, '046, '481, '916 and '106 (excluding those portions pertaining to the use code U-3697 (treatment of CF in a patient age 1 month to <4 months who has at least one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data using the composition recited in claim 1 of US 11752106)) patents' under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patents are invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Ivacaftor Oral Granules, 25 mg, 50 mg and 75 mg per unit dose packet, under this ANDA. You have notified the Agency that Lupin complied with the requirements of section 505(j)(2)(B) of the FD&C

Act. Litigation was initiated within the statutory 45-day period against Lupin for infringement of the '206, '046 and '481 patents in the United States District Court for the District of Delaware [Vertex Pharmaceuticals Incorporated v. Lupin Limited and Lupin Pharmaceuticals, Inc., Civil Action No. 22-00966]. Although this litigation remains ongoing, the 30-month period identified in section 505(j)(5)(B)(iii) of the FD&C Act, during which FDA was precluded from approving your ANDA, has expired.

With respect to portions of the '106 patent pertaining to (b) (4)
(b) (4)
(b) (4) your ANDA contains statements under
section 505(j)(2)(A)(viii) of the FD&C Act (b) (4)
(b) (4)

With respect to the '770 patent, the Agency has determined that information on this patent was submitted to the Agency by the new drug application (NDA) holder (a) after the date of the submission of your ANDA, and (b) more than 30 days after the patent was required to be submitted under 21 CFR 314.53. Therefore, under 21 CFR 314.94(a)(12)(vi), no person with an appropriate patent certification at the time of the submission of the patent was required to submit an amended patent certification to address the '510 and '511 patents. You elected not to submit an amended patent certification with respect to these patents.

Please note that if FDA requires a Risk Evaluation and Mitigation Strategy (REMS) for a listed drug, an ANDA referencing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL

Under applicable statutes, regulations, and guidances, if your ANDA receives final approval, it may be subject to certain requirements and recommendations post approval, including requirements regarding changes to approved ANDAs, postmarketing reporting, promotional materials, and annual facility fees, among others. For information on post-approval requirements and recommendations for ANDAs and a list of resources for ANDA holders, we refer you to <https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/requirements-and-resources-approved-andas>.

RESUBMISSION

To request final approval, please submit an amendment titled "FINAL APPROVAL REQUESTED" with enough time to permit FDA review prior to the date you believe that your ANDA will be eligible for final approval. A request for final approval that contains no new data, information, or other changes to the ANDA generally requires a period of 3 months for Agency review. Accordingly, such a request for final approval should be submitted no later than 3 months prior to the date on which you seek approval. A request for final approval that contains substantive changes to this ANDA or changes in

the status of the manufacturing and testing facilities' compliance with cGMPs will be classified and reviewed according to OGD policy in effect at the time of receipt. Applicants should review available agency guidance for industry related to amendments under the generic drug user fee program to determine the duration of Agency review needed to review the changes submitted. As part of this consideration, applicants should monitor any changes to the RLD that occur after tentative approval, including changes in labeling, patent or exclusivity information, or marketing status. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

The amendment requesting final approval should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, settlement or licensing agreement, or other information described in 21 CFR 314.107, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, e.g., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a "FINAL APPROVAL REQUESTED."

In addition to the amendment requested above, the Agency may request, at any time prior to the date of final approval, that you submit an additional amendment containing information as specified by the Agency. Failure to submit either or, if requested, both types of amendments described above may result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final Agency approval under section 505(j) of the FD&C Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the FD&C Act. Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under section 505(j) of the FD&C Act, and will not be listed in the Orange Book. Should you believe that there are grounds for issuing the final approval letter prior to August 5, 2027, you should amend your ANDA accordingly.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Warren Simmons, Regulatory Project Manager, at (240) 402 - 6258.

Sincerely yours,

{See appended electronic signature page}

For Edward M. Sherwood
Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

¹ The Agency notes that the '916 and '106 patents were submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to these patents would not create a statutory stay of approval.



Catherine
Poole

Digitally signed by Catherine Poole

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