U.S. FOOD & DRUG ADMINISTRATION

ANDA 216064

**ANDA APPROVAL/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 12, 2021, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Valbenazine Capsules, 40 mg, 60 mg, and 80 mg.

Reference is also made to the tentative approval letter issued by this office on March 24, 2023, 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 Valbenazine Capsules, 40 mg, 60 mg, and 80 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Ingrezza Capsules, 40 mg, 60 mg, and 80 mg, of Neurocrine Biosciences, Inc. (Neurocrine).

However, we are unable to grant final approval to your Valbenazine Capsules, 60 mg, at this time because of the exclusivity issue noted below. Therefore, your ANDA is **approved** insofar as it pertains to Valbenazine Capsules, 40 mg and 80 mg. Your Valbenazine Capsules, 60 mg 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.

The reference listed drug (RLD) upon which you have based your ANDA, Neurocrine's Ingrezza Capsules, 40 mg, 60 mg, and 80 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.S. Patent Number | Expiration Date |
|---|---|
| 8,039,627 (the '627 patent) | April 11, 2031 |
| 8,357,697 (the '697 patent) | November 8, 2027 |
| 10,065,952 (the '952 patent) | October 28, 2036 |
| 10,844,058 (the '058 patent) | October 28, 2036 |
| 10,851,103 (the '103 patent) | October 28, 2036 |
| 10,851,104 (the '104 patent) | October 28, 2036 |
| 10,857,137 (the '137 patent) | October 10, 2037 |
| 10,857,148 (the '148 patent) | October 10, 2037 |
| 10,874,648 (the '648 patent) | October 10, 2037 |
| 10,906,902 (the '902 patent) | December 22, 2036 |
| 10,906,903 (the '903 patent) | December 22, 2036 |
| 10,912,771 (the '771 patent) | October 10, 2037 |
| 10,919,892 (the '892 patent) | December 22, 2036 |
| 10,940,141 (the '141 patent) | August 10, 2040 |
| 10,952,997 (the '997 patent) | October 10, 2037 |

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|---|---|
| 10,993,941 (the '941 patent) | October 10, 2037 |
| 11,026,931 (the '931 patent) | August 14, 2039 |
| 11,026,939 (the '939 patent) | September 18, 2038 |
| 11,040,029 (the '029 patent) | October 10, 2037 |
| 11,311,532 (the '532 patent) | September 18, 2038 |
| 11,439,629 (the '629 patent) | October 10, 2037 |
| 11,654,142 (the '142 patent) | November 14, 2038 |

With respect to: 1) the '629 and '142 patents and 2) portions of the ‘697, ‘952, ‘058, ‘103, ‘104, ‘648, ‘771, ‘939, and ‘532 patents pertaining to the use code U-3055 (a method of treating Huntington’s chorea), your ANDA contains statements under section 505(j)(2)(A)(viii) of the FD&C Act that these are method-of-use patents that do not claim any indication or other conditions of use for which you are seeking approval under your ANDA.

With respect to: 1) the ‘627, ‘137, ‘148, ‘902, ‘903, ‘892, ‘141, ‘997, ‘941, ‘931, and ‘029 patents and 2) the ‘697, ‘952, ‘058, ‘103, ‘104, ‘648, ‘771, ‘939, and ‘532 patents[1] (excluding those portions pertaining to the use code U-3055 (a method of treating Huntington’s chorea) your ANDA contains paragraph IV certifications 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 Valbenazine Capsules, 40 mg, 60 mg, and 80 mg, under this ANDA. You have notified the Agency that Lupin Limited (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 '627, '697, '952, '058, '103, '104, '137, '148, '648, '902, '903, '771, '892, '141, '997, '941, '931, '939, and '029 patents in the United States District Court for the District of Delaware [Neurocrine Biosciences, Inc. v. Lupin Limited and Lupin Pharmaceuticals, Inc., et al, Civil Action No. 21-01042 (consolidated)]. You have also notified the Agency that this case was dismissed.

However, we are unable to grant final approval to with respect to the 60 mg strength product at this time. Prior to the submission of your ANDA, another applicant or applicants submitted a substantially complete ANDA providing for Valbenazine Capsules, 60 mg and containing a paragraph IV certification. Your ANDA for this strength will be eligible for final approval on the date that is 180 days after the commercial marketing date identified in section 505(j)(5)(B)(iv) of the FD&C Act.

Upon the foregoing, your ANDA is **approved** insofar as it pertains to the 40 mg and 80 mg products. Your 60 mg, product is **tentatively approved**.

## I. Approval of Valbenazine Capsules, 40 mg and 80 mg

With respect to 180-day generic drug exclusivity, we note that Lupin was one the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification for Valbenazine Capsules, 40 mg and 80 mg. Therefore, with this approval, Lupin is eligible for 180 days of shared generic drug exclusivity for Valbenazine Capsules, 40 mg and 80 mg. FDA notes that after issuance of this approval letter, eligibility for 180-day exclusivity is subject to future events that may result in forfeiture of exclusivity under section 505(j)(5)(D) of the FD&C Act. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, begins to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA notifying the Agency within 30 days of the date of the first commercial marketing of this drug product or the RLD. If you do not notify the Agency within 30 days, the date of first commercial marketing will be deemed to be the date of the drug product's approval. See 21 CFR 314.107(c)(2).

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.

## COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standard for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise official USP monographs. More information on the USP-NF is available on USP's website as https://www.uspnf.com/.

## II. Tentative Approval of Valbenazine Capsules, 60 mg

Our decision to tentatively approve your Valbenazine Capsules, 60 mg, is based upon information currently available to the agency (i.e., data in your ANDA and the status of current good manufacturing practice (cGMP) of the facilities used in the manufacture and testing of the drug product). This decision is subject to change on the basis of new information that may come to our attention.

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.

## 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, i.e., 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 "MINOR/MAJOR AMENDMENT TO ORIGINAL #2 – 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.

**REQUIREMENTS AND RECOMMENDATIONS POST APPROVAL**

Under applicable statutes, regulations, and guidances, your ANDA 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.

For further information on the status of this ANDA or upon submitting an amendment to the ANDA, please contact Catherine Morales, Regulatory Project Manager, at (301) 796 - 3585.

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] With respect to the 40 mg and 80 mg strengths, the Agency notes that the '941, '931, '939, '029 and '532 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. With respect to the 60 mg strength, the Agency notes that the '532 patent was submitted to the Agency after submission of your ANDA. Litigation, if any, with respect to this patent would not create a statutory stay of approval.

John Ibrahim

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