



ANDA 218796

**ANDA TENTATIVE APPROVAL**

Biophore Pharma Inc.  
U.S. Agent for Zenara Pharma Private Limited  
4262 US Highway 1, Suite A  
Monmouth Junction, NJ 08852  
Attention: Harsha Vemuri  
U.S. Agent

Dear Harsha Vemuri:

This letter is in reference to your abbreviated new drug application (ANDA) received for review on August 14, 2023, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) for Pitolisant Tablets, 4.45 mg and 17.8 mg.

Reference is also made to the complete response letter issued by this office on June 11, 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 Pitolisant Tablets, 4.45 mg and 17.8 mg to be bioequivalent and therapeutically equivalent to the reference listed drug (RLD), Wakix Tablets, 4.45 mg and 17.8 mg, of Harmony Biosciences Management, Inc. (Harmony) NDA - 211150.

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, Harmony's Wakix Tablets, 4.45 mg and 17.8 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> |
|-----------------------------|------------------------|
| 8,207,197 (the '197 patent) | March 7, 2030          |
| 8,354,430 (the '430 patent) | February 6, 2026       |
| 8,486,947 (the '947 patent) | September 26, 2029     |

With respect to: 1) the '197 patent and 2) the '430 and '947 patents (excluding portions pertaining to the use code U-1101 (method of treating excessive daytime sleepiness in patients with narcolepsy), 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 Pitolisant Tablets, 4.45 mg and 17.8 mg, under this ANDA. You have notified the Agency that Zenara Pharma Private Limited (Zenara) 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 Zenara for infringement of the '197, '430, and '947 patents in the United States District Court for the District of Delaware [Harmony Biosciences, LLC, Bioprojet Société Civile De Recherche and Bioprojet Pharma SAS v. Zenara Pharma Private Limited, et al., Civil Action No. 23-01340].

Therefore, final approval cannot be granted until:

- the expiration of the 7.5-year period provided for in sections 505(j)(5)(B)(iii) and 505(j)(5)(F)(ii) of the FD&C Act,
  - the date the court decides<sup>1</sup> that the '197, '430, and '947 patents are invalid or not infringed (see sections 505(j)(5)(B)(iii)(I), (II), and (III) of the FD&C Act), or
  - the '197, '430, and '947 patents have expired, and
- The Agency is assured there is no new information that would affect whether final approval should be granted.

With respect to the '430 and '947 patents pertaining to the use code U-1101 (method of treating excessive daytime sleepiness in patients with narcolepsy), 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 for which you are seeking approval under your ANDA.

The RLD upon which you have based your ANDA, Harmony's Wakix Tablets, 4.45 mg and 17.8 mg, is subject to a period of exclusivity. As noted in the Orange Book, the ODE-331 exclusivity is scheduled to expire on October 13, 2027. Your ANDA contains a statement that you do not seek to market Pitolisant Tablets, 4.45 mg and 17.8 mg, prior

to the expiration of this exclusivity. Therefore, final approval cannot be granted until the ODE-331 exclusivity has expired, currently October 13, 2027.

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 October 13, 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 Pamela Morgan, Regulatory Project Manager, at (301) 837 - 7611.

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

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<sup>1</sup> This decision may be either a decision of the district court or the court of appeals, whichever court is the first to decide that the patent is invalid or not infringed.



Paul  
Levine

Digitally signed by Paul Levine

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