BLA 761204

BLA APPROVAL

Amicus Therapeutics US, LLC
Attention: Jamie L. Gault, RAC
Vice President, Global Regulatory Affairs
3675 Market Street
Philadelphia, PA 19104

Dear Jamie Gault:

Please refer to your biologics license application (BLA) dated and received July 29, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for Pombiliti (cipaglucosidase alfa-atga) injection.

We acknowledge receipt of your major amendment dated April 29, 2022, which extended the goal date by three months.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2224 to Amicus Therapeutics US, LLC, Philadelphia, Pennsylvania, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Pombiliti (cipaglucosidase alfa-atga). Pombiliti is indicated, in combination with Opfolda, for the treatment of adult patients with late-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) weighing ≥40 kg and who are not improving on their current enzyme replacement therapy (ERT).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture cipaglucosidase alfa-atga drug substance and drug product at WuXi Biologics Co., Ltd. in Wuxi, Jiangsu, China (FEI 3010606982). The final formulated drug product will be labeled and packaged at (b) (4) (b) (4). You may label your product with the proprietary name, Pombiliti, and market it in a single-dose vial containing 105 mg lyophilized powder for injection.

DATING PERIOD

The dating period for Pombiliti shall be 36 months from the date of manufacture when stored at 2 to 8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) from the date of manufacture when stored (b) (4).

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Pombiliti to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Pombiliti, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the

[1] See http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm
[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761204**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Pombiliti was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of the biologic in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4322-1 To perform extractables/leachables studies and risk assessments to evaluate leachables from the container closure system(s) and manufacturing product contact surfaces of cipaglucosidase alfa drug substance and drug product and assess the potential impact of leachables on product quality at the end of drug product shelf-life. The analyses will be performed using drug substance and drug product lot(s) and/or representative samples ([redacted] (b) (4), if justified) analyzed at appropriate time points, including at the end of drug product shelf life. Appropriate methods will be used to detect, identify, and quantify organic non-volatile, volatile and semi-volatile species, and metals. Characterization of the potential impact of leachables on product quality will be assessed using adequate analytical methods. Complete data and the risk evaluation for the potential impact of leachables on product safety and quality will be provided in the final study report per 21 CFR 601.12.

The timetable you submitted on August 3, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2023

4322-2 To develop, validate, and implement a test method with justified numerical acceptance criteria for control of cipaglucosidase alfa kinetic parameters during drug product release and stability testing. Critical kinetic parameters (e.g., K_m, K_{cat}, etc.,) will be determined, justified, and included in the control strategy. If applicable, justification and data supporting [redacted] (b) (4) will be provided. The method validation report for the enzyme kinetic assay, the revised drug product release and stability specifications, and all supporting studies and data will be provided in a final study report per 21 CFR 601.12.

The timetable you submitted on August 3, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2024

4322-3 To develop an endotoxin method for the drug product which mitigates the low endotoxin recovery (LER) effect, to submit method qualification results with three lots of drug product and provide results of an LER study performed with the updated method with three lots of drug product.

The timetable you submitted on August 3, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2024

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Jenny Doan, Regulatory Project Manager, at (301) 796-1023.

Sincerely,

{See appended electronic signature page}

Janet W Maynard, MD, MHS
Director
Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:
- Content of Labeling
  - Prescribing Information
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JANET W MAYNARD
09/28/2023 06:39:41 AM