BLA 761177

CORRECTED BLA APPROVAL

Ascendis Pharma Endocrinology Division A/S
Attention: Jessica M. Peng, PharmD
Regulatory Affairs Manager, Ascendis Pharma, Inc.
500 Emerson Street
Palo Alto, CA 94301

Dear Dr. Peng:

Please refer to your biologics license application (BLA) dated and received June 25, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Skytrofa (lonapegsomatropin-tcgd) for injection.

We also refer to our approval letter dated August 25, 2021, which contained the following error: missing auto-injector box label.

This corrected action letter incorporates the correction of the error. The effective action date will remain August 25, 2021, the date of the original letter.

We also acknowledge receipt of your major amendment dated May 11, 2021, which extended the goal date by three months.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2165 to Ascendis Pharma Endocrinology Division A/S, Palo Alto, CA, 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 Skytrofa (lonapegsomatropin-tcgd). Skytrofa is indicated for the treatment of pediatric patients 1 year and older who weigh at least 11.5 kg and have growth failure due to inadequate secretion of endogenous growth hormone (GH).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture lonapegsomatropin-tcgd drug substance at FUJIFILM Diosynth Biotechnologies UK Ltd in Belasis Avenue Billingham TS23 1LH, United Kingdom. The final formulated drug product will be manufactured, filled, labeled, and packaged at the following locations:

- Vetter Pharma-Fertigung GmbH & Co. KG, Ravensburg, Germany (Manufacture dual chamber cartridge)

- Sharp Corporation, Allentown, PA (Packaging, [redacted] and Labeling)

- B. Braun Medical Industries Sdn. Bhd., Pulau Pinang, Malaysia (Manufacturing of 510(k) approved injection needle)

- Phillips-Medisize A/S, Struer, Denmark (Manufacturing and Packaging, GH auto-injector)

You may label your product with the proprietary name, Skytrofa, and market it in 3 mg, 3.6 mg, 4.3 mg, 5.2 mg, 6.3 mg, 7.6 mg, 9.1 mg, 11 mg, and 13.3 mg of lyophilized powder for reconstitution and water for injection in a dual chamber cartridge for single-dose.

DATING PERIOD

The dating period for Skytrofa shall be 36 months months from the date of manufacture when stored at 2-8°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 [redacted] months from the date of manufacture when stored at [redacted]°C [redacted] For the human growth hormone (hGH) intermediate, the dating period shall be [redacted] months from the date of manufacture when stored at [redacted]°C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Skytrofa 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 Skytrofa, 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 with minor editorial revisions listed below and reflected in the enclosed labeling.

- Initial U.S. Approval date and Revision date in the Prescribing Information have been updated to reflect the date of approval of this application.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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, Instructions for Use, and Quick Reference Guide). 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 submitted on August 17, 2021, as soon as they are available [e.g., changes consistent with annual reportable changes under 21 CFR 6101.12(d)], but no more than 30 days after they are printed. Please submit these labeling electronically according to the 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 761177**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Skytrofa 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.

[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.

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:

4037-1 Provide the shipping validation report of the bulk drug product in dual-chamber cartridges shipped from (b) (4) during winter and summer conditions

The timetable you submitted on March 4, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2023

4037-2 Compliance to IEC 60601-1-8 for device alarms

The timetable you submitted on July 8, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2022

4037-3 Validation of Corrective Actions/Preventive Actions (CAPA) for (b) (4) (b) (4) assembly issue

The timetable you submitted on July 8, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2021

Submit chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and

final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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 for licensed biological products (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 for licensed biological products (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:

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

[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

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 Sejal Kiani, Regulatory Project Manager, at (301) 796-6445.

Sincerely,

{See appended electronic signature page}

Lisa B. Yanoff, MD
Deputy Director (Acting)
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Instructions for Use
  - Quick Reference Guide
- 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/

LISA B YANOFF
08/26/2021 02:50:07 PM