

BLA 761145

**BLA APPROVAL**

Janssen Biotech, Inc.  
Attention: Melanie Rothschild, MBA  
Associate Director, Regulatory Affairs  
920 Route 202 South  
Raritan, NJ 08869

Dear Ms. Rothschild:<sup>1</sup>

Please refer to your biologics license application (BLA) dated July 12, 2019, received July 12, 2019, and your amendments, submitted under section 351(a) of the Public Health Service Act for Darzalex Faspro (daratumumab and hyaluronidase-fihj), for subcutaneous injection.

We have approved your BLA for Darzalex Faspro (daratumumab and hyaluronidase-fihj) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, daratumumab and hyaluronidase-fihj under your existing Department of Health and Human Services U.S. License No.1864. Darzalex Faspro (daratumumab and hyaluronidase-fihj) is indicated for treatment of adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
- as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

### **MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture daratumumab drug substance at <sup>(b) (4)</sup> Under this license, you

<sup>1</sup> We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

are approved to manufacture hyaluronidase drug substance at (b) (4) (b) (4). The final formulated drug product will be manufactured, filled, labeled, and packaged at (b) (4) (b) (4). You may label your product with the proprietary name, Darzalex Faspro, and market it in a 1,800 mg daratumumab and 30,000 Units hyaluronidase per 15 mL (120 mg/2,000 Units per mL) Injection in a single-dose vial.

### **DATING PERIOD**

The dating period for Darzalex Faspro shall be 12 months from the date of manufacture when stored at 2°C 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 daratumumab drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) (b) (4). The dating period for your hyaluronidase drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) (b) (4).

We have approved the stability protocol in your license application for the purpose of extending the expiration dating period of your hyaluronidase drug substance under 21 CFR 601.12.

### **FDA LOT RELEASE**

You are not currently required to submit samples of future lots of Darzalex Faspro 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 Darzalex Faspro, or in the manufacturing facilities, will require the submission of information to your biologics license application 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, as described at FDA.gov.<sup>2</sup> Content of labeling must be identical to the enclosed labeling (text for the

<sup>2</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Prescribing Information, Patient Package Insert). 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*.<sup>3</sup>

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 carton and container labeling submitted on March 9 and 20, 2020, as soon as they are available, 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 761145.**” Approval of this submission by FDA is not required before the labeling is used.

### **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 commitment:

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<sup>3</sup> 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>.

3835-1 Confirm the effectiveness of updates to the daratumumab SC drug substance manufacturing process to ensure the continued ability to meet expectations during drug product shelf life for levels of sub-visible particles. The effectiveness of the modifications should be supported by real-time and accelerated drug product stability data between material produced by the current manufacturing process and the improved process. Provide the statistical plans used to evaluate the data, as well as validation and supportive data for any process updates and manufacturing control strategy updates in the final report.

The timetable you submitted on April 9, 2020, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2022

Submit nonclinical and 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. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Patient Package Insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.<sup>4</sup>

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<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup> For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.<sup>6</sup>

### **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

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

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<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

<sup>6</sup> <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

## **MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at [FDA.gov](http://FDA.gov).<sup>7</sup>

If you have any questions, call Kimberly Scott, Senior Regulatory Project Manager, at (240) 402-4560.

Sincerely,

*{See appended electronic signature page}*

Nicole Gormley, MD  
Division Director (Acting)  
Division of Hematologic Malignancies II  
Office of Oncologic Diseases  
Center for Drug Evaluation and Research

### ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

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<sup>7</sup> <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>

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**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.**  
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/s/  
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NICOLE J GORMLEY  
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