BLA 761433

BLA APPROVAL

Janssen Biotech, Inc.
Attention: Yvonne Wu, Ph.D.
Associate Director, Global Regulatory Affairs
920 U.S. Route 202
Raritan, NJ 08869

Dear Dr. Wu:

Please refer to your biologics license application (BLA) received June 14, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) injection.

We acknowledge receipt of your resubmission dated March 21, 2025, which constituted a complete response to our December 13, 2024, action letter.

We acknowledge receipt of your major amendment dated September 4, 2025, which extended the goal date by three months.

LICENSING

We have approved your BLA for Rybrevant Faspro (amivantamab and hyaluronidase-lpuj) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Rybrevant Faspro under your existing Department of Health and Human Services U.S. License No. 1864.

Rybrevant Faspro is indicated for the following indications:

- In combination with lazertinib for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with EGFR exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.
- In combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 19 deletions or exon 21 L858R substitution mutations, whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor.
- In combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test.
- As a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an

FDA approved test, whose disease has progressed on or after platinum-based chemotherapy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture amivantamab drug substance [redacted] at Janssen Sciences Ireland UC, Barnahely, Ringaskiddy, Co. Cork, Ireland. The final formulated drug product will be manufactured, filled, labeled, and packaged at [redacted] You may label your product with the proprietary name, Rybrevant Faspro, and market it in single-dose vials at 10.0 and 14.0 mL nominal fill volumes:

- The 10.0 mL vials contain 1,600 mg amivantamab (160 mg/mL) and 20,000 units hyaluronidase (2,000 U/mL)
- The 14.0 mL vials contain 2,240 mg amivantamab (160 mg/mL) and 28,000 units hyaluronidase (2,000 U/mL)

DATING PERIOD

The dating period for Rybrevant Faspro shall be 18 months from the date of manufacture when stored at 5 ± 3 °C, protected from light. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your amivantamab drug substance is [redacted] months at [redacted]

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your [redacted] amivantamab drug substance, and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Rybrevant 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 Rybrevant Faspro, 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 and 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 (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 guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761433**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Rybrevant Faspro 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.

[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.

We are waiving the pediatric study requirement for this application because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients and is not likely to be used in a substantial number of pediatric patients.

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

We remind you of your postmarketing commitments:

4947-1 Re-evaluate and update the acceptance criterion of (b) (4) for amivantamab drug substance after 30 commercial drug substance batches have been released. Submit the (b) (4) acceptance criterion reanalysis data and update the amivantamab drug substance release specification and other relevant BLA sections (e.g., justification of specification, protocols).

The timetable you submitted on December 4, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2026

4947-2 To perform a pilot scale study for each parental antibody (b) (4) and compare the product quality data against historical data to support the proposed limit of in vitro cell age (LIVCA) for (b) (4)

The timetable you submitted on December 4, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2026

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/subjects 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 601.12(f)(4)]. 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:

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, email the Regulatory Project Manager for this application.

If you have any questions, contact Monica Estrada, Regulatory Project Manager, at Monica.Estrada@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Paz Vellanki, MD, PhD
Supervisory Associate Director
Division of Oncology 2
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- 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/

PAZ J VELLANKI
12/17/2025 04:24:10 PM