# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

## *APPLICATION NUMBER:*

## 761210Orig1s000

| | |
|---|---|
| ***Trade Name:*** | RYBREVANT |
| ***Generic or Proper Name:*** | amivantamab-vmjw injection, for intravenous use |
| ***Sponsor:*** | Janssen Biotech, Inc |
| ***Approval Date:*** | May 21, 2021 |
| ***Indication:*** | indicated for treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. |

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***APPLICATION NUMBER:***

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# APPROVAL LETTER

U.S. FOOD & DRUG ADMINISTRATION

BLA 761210

**BLA ACCELERATED APPROVAL**

Janssen Biotech, Inc.
Attention: Julie Brennan, M.S., RAC
Director, Global Regulatory Affairs
920 U.S. Route 202
Raritan, NJ 08869

Dear Ms. Brennan:

Please refer to your biologics license application (BLA) dated November 24, 2020, received November 24, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for RYBREVANT (amivantamab-vmjw) injection, for intravenous use.

## LICENSING

We have approved your BLA for RYBREVANT (amivantamab-vmjw) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, RYBREVANT under your existing Department of Health and Human Services U.S. License No. 1864. RYBREVANT is indicated for treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (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 (b) (4) amivantamab-vmjw drug substance at Janssen Sciences Ireland, UC in Barnahely, Ringaskiddy, County Cork, Ireland. The final formulated product will be manufactured, filled, labeled, and packaged at Cilag AG, Schaffhausen, Switzerland. You may label your product with the proprietary name RYBREVANT and will market it as a 350 mg/7mL solution in a single-dose vial.

## DATING PERIOD

The dating period for RYBREVANT shall be 18 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 (b) (4) shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C. The dating period for your (b) (4)

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

Results of ongoing stability should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your (b) (4) , 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 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, 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 AND LABELING

We have completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 601.41), effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

## 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.[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

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.[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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (April 2018, Revision 5)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761210**." Approval of this submission by FDA is not required before the labeling is used.

## ADVISORY COMMITTEE

Your application for amivantamab-vmjw was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of amivantamab-vmjw in the proposed indication. The application also did not raise significant safety or efficacy issues.

## ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 601.41, require further adequate and well-controlled clinical trials to verify and describe clinical benefit. You are required to conduct such clinical trials with due diligence. If postmarketing clinical trials fail to verify clinical benefit or are not conducted with due diligence, we may, following a hearing in accordance with 21 CFR 601.43(b), withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated May 17, 2021. This requirement, along with required completion dates, is listed below.

4070-1 Submit the final report, including datasets for progression free survival, overall response rate, duration of response, and overall survival from a randomized clinical trial to verify and confirm the clinical benefit of amivantamab-vmjw for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations. This could be from the ongoing clinical trial entitled, "A Randomized, Open-label Phase 3 Study of Combination Amivantamab and Carboplatin-Pemetrexed Therapy, Compared With Carboplatin-Pemetrexed, in

[2] 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.

Patients With EGFR Exon 20ins Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer."

Final Protocol Submission: 7/2020
Trial Completion: 8/2022
Final Report Submission: 2/2023

Submit clinical protocols to your IND 135405 for this product. In addition, under 21 CFR 601.70, you should include a status summary of each requirement in your annual report 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.

Submit final reports to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart E Postmarketing Requirement**."

## 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.

We are waiving the pediatric study requirement for this application because the necessary studies are impossible or highly impracticable as NSCLC does not occur in children.

## POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4070-2 Submit the final results, including datasets for overall response rate and duration of response, from CHRYSALIS titled " A Phase 1, First-in-Human, Open-Label, Dose Escalation Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants with Advanced Non-Small Cell Lung Cancer" to further characterize the clinical benefit of amivantamab-vmjw for the treatment of patients with NSCLC with EGFR exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy to provide a more precise estimation of the blinded independent central review-assessed overall response rate and duration of response after all responders in the relevant patient population

(approximately 128 patients) have been followed for at least 6 months from the date of initial response (or until disease progression, whichever comes first). These results may inform product labeling.

The timetable you submitted on May 17, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2021

4070-3 Submit a final report containing data from clinical trials enrolling a sufficient representation of Black or African American patients that is reflective of the U.S. population of patients with EGFR exon 20 insertion mutated NSCLC to further characterize the safety and efficacy of amivantamab-vmjw in Black or African American patients with EGFR exon 20 insertion mutated NSCLC.

The timetable you submitted on May 17, 2021, states that you conduct this study according to the following schedule:

Draft Analysis Plan Submission: 10/2022
Final Analysis Plan Submission: 1/2023
Final Report Submission: 4/2023

4070-4 Submit a summary of the final report of an analytical and clinical validation study, using clinical trial data, that is adequate to support labeling of a tissue-based in vitro diagnostic device that demonstrates the device is essential to the safe and effective use of amivantamab-vmjw for patients diagnosed with NSCLC with EGFR exon 20 insertion mutations. The results of the validation study may inform product labeling.

The timetable you submitted on May 17, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 8/2021

Submit 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 Final Report**," or "**Postmarketing Commitment Correspondence**."

## PROMOTIONAL MATERIALS

Under 21 CFR 601.45, you are required to submit, during the application pre-approval review period, all promotional materials, including promotional labeling and advertisements, that you intend to use in the first 120 days following marketing approval (i.e., your launch campaign). If you have not already met this requirement, you must immediately contact the Office of Prescription Drug Promotion (OPDP) at (301) 796-1200. Please ask to speak to a regulatory project manager or the appropriate reviewer to discuss this issue.

As further required by 21 CFR 601.45, submit all promotional materials that you intend to use after the 120 days following marketing approval (i.e., your post-launch materials) at least 30 days before the intended time of initial dissemination of labeling or initial publication of the advertisement. We ask that each submission include a detailed cover letter together with three copies each of the promotional materials, annotated references, and approved Prescribing Information, Medication Guide, and Patient Package Insert (as applicable).

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]

## 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:

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

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 molecular entities and new biologics 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, contact the Regulatory Project Manager for this application.

If you have any questions, please email Sharon Sickafuse, Senior Regulatory Health Project Manager, at sharon.sickafuse@fda.hhs.gov.

Sincerely,

*{See appended electronic signature page}*

Julia Beaver, M.D.
Acting Deputy Director
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- Carton and Container Labeling

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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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JULIA A BEAVER
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