BLA 761210/S-003

SUPPLEMENT APPROVAL/
FULFILLMENT OF POSTMARKETING
REQUIREMENT

Janssen Biotech, Inc.
Attention: Aaron Seto, Ph.D., RAC
Associate Director, Global Regulatory Affairs
c/o Janssen Research & Development, LLC
920 U.S. Route 202
Raritan, NJ 08869

Dear Dr. Seto:

Please refer to your supplemental biologics license application (sBLA), dated and received September 28, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Rybrevant (amivantamab-vmjw) injection.

This Prior Approval supplemental biologics license application provides for:

- A new indication of amivantamab in combination with carboplatin and pemetrexed for the first-line 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.
- Revisions to US Prescribing Information (USPI) to support the fulfillment of the subpart E postmarketing requirement and traditional approval of amivantamab 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.

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:

- Insertion of March 2024 revision date in final Rybrevant USPI and Patient Information labeling.

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, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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*.[2]

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

SUBPART E FULFILLED

We approved this BLA under the regulations at 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills your commitments made under 21 CFR 601.41.

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

[1] 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 https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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 necessary studies are impossible or highly impracticable as NSCLC does not occur in children.

FULFILLMENT OF POSTMARKETING REQUIREMENT

We have received your submission dated September 28, 2023, containing the final report for the following postmarketing requirement listed in the May 21, 2021, approval letter for BLA 761210.

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

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there is a postmarketing commitment listed in the May 21, 2021, approval letter that is still open.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4597-1 Complete clinical trial PAPILLON (NCT04538664) and include the results of the final overall survival analysis, once the anticipated 210 death events have occurred, to further characterize the clinical benefit of amivantamab in combination with carboplatin and pemetrexed, for the first line treatment of adult patients with metastatic non-small cell lung cancer harboring epidermal growth factor receptor exon 20 insertion mutations.

The timetable you submitted on February 28, 2024, states that you will conduct this study according to the following schedule:

Final Protocol Submission: 09/2022 (Completed)
Trial Completion: 09/2025
Final Report Submission: 03/2026

Submit the datasets with the final report submission.

4597-2 Conduct an integrated analysis containing data from clinical trials and other data sources, such as real-world evidence and post-marketing clinical trial reports, to further characterize the efficacy and safety of amivantamab in combination with carboplatin and pemetrexed in patients ages 75 years and older, Black or African American patients, and patients of Latino ethnicity, diagnosed with metastatic NSCLC harboring EGFR exon 20 insertion mutations.

The timetable you submitted on February 28, 2024, states that you will conduct this study according to the following schedule:

Draft Protocol Submission (Analysis Plan):	10/2024
Final Protocol Submission (Analysis Plan):	04/2025
Study Completion:	06/2028
Final Report Submission:	12/2028

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit clinical protocols to your IND 135405 for this product. 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/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]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, contact Ashley Lane, Senior Regulatory Health Project Manager, at Ashley.Lane@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Harpreet Singh, M.D.
Director
Division of Oncology 2
Office of Oncologic Diseases
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

[3] For the most recent version of a guidance, check the FDA guidance web page athttps://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

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/s/

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