BLA 761263/S-006

ACCELERATED APPROVAL

Genentech, Inc.
Attention: Ardelle Ying, MD
Senior Regulatory Program Director
1 DNA Way
Southern San Francisco, CA 94080

Dear Dr. Ying:

Please refer to your supplemental biologics license application (sBLA), dated and received November 22, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Lunsumio Velo (mosunetuzumab-axgb) injection, for subcutaneous use.

We acknowledge receipt of your major amendment dated June 20, 2025, which extended the goal date by three months.

This Prior Approval supplemental biologics license application provides for a new subcutaneous (SC) route of administration of mosunetuzumab-axgb for the treatment of adult patients with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

In addition, the product labeling for Lunsumio (mosunetuzumab-axgb) injection for intravenous (IV) use was updated to include the following:

- Addition of new Warning and Precaution, Section 5.7, Risk of Medication Errors with Incorrect Product Use
- Updates to Dosing and Administration, Section 2.1, Important Dosing Information to differentiate Lunsumio (IV administration) and Lunsumio Velo (SC administration).
- Other changes include:
    - Updates to Dosage and Administration, Section 2.3 Recommended Premedication to designate dexamethasone as the preferred corticosteroid
    - Revision to Warning and Precaution, Section 5.1 Cytokine Release Syndrome (CRS) to correct the rate of recurrent CRS.
    - Update to Warning and Precaution, Section 5.2 Neurologic Toxicity, including Immune Effector Cell-Associated Neurologic Toxicity (ICANS)
    - Minor edits throughout product labeling to clarify the route of administration.

APPROVAL & 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] that is identical to the enclosed labeling (text for the Prescribing Information and Medication Guide) 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).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling submitted on October 22, 2025, 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 761263/S-006**." Approval of this submission by FDA is not required before the labeling is used.

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

ACCELERATED APPROVAL REQUIREMENTS

Pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and 21 CFR 601.41, you are required to conduct further adequate and well-controlled clinical trials intended 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, including with respect to the conditions set forth below, we may withdraw this approval. We remind you of your postmarketing requirement specified in your submission dated December 8, 2025. This requirement is listed below.

4945-1 Complete a randomized clinical trial intended to verify and describe the clinical benefit of mosunetuzumab in patients with follicular lymphoma. The trial should randomize patients with relapsed or refractory follicular lymphoma to receive mosunetuzumab in combination with lenalidomide or rituximab in combination with lenalidomide. The primary endpoint should be progression-free survival, with secondary endpoints that include response rate and overall survival. The trial should enroll a sufficiently representative study population to reflect the racial and ethnic populations to better reflect the U.S. patient population with follicular lymphoma and allow for interpretation of the results in these patient populations.

If the trial evaluates mosunetuzumab by intravenous injection, submit the final report of integrated studies and data to verify and further characterize the comparability, efficacy, and safety of mosunetuzumab by subcutaneous injection in combination with lenalidomide, to mosunetuzumab by intravenous injection in combination with lenalidomide. The final protocol should include the integrated comparative assessment plan.

Draft Protocol Submission (Including Integrated Analysis Plan):	01/2026
Final Protocol Submission (Including Integrated Analysis Plan):	05/2026
Trial Completion:	09/2026
Final Report Submission:	03/2027

Submit clinical protocols to your IND 120651 for this product. FDA considers the term final to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.

You must submit reports of the progress of each clinical trial under section 506(c) (listed above) to this BLA approximately every 180 days (see section 506B(a)(2) of the FDCA) (hereinafter “180-day reports”).

You are required to submit two 180-day reports per year for each open study or clinical trial required under section 506(c). One report will be a standalone submission and the other report will be combined with your application's annual status report (ASR) required under section 506B(a)(1) of the FDCA and 21 CFR 601.70. The standalone 180-day report will be due 180 days after the date of approval of the original BLA (with a 60-day grace period). Submit the other 180-day report with your application's ASR. Submit both of these 180-day reports each year until the final report for the corresponding study or clinical trial is submitted.[3] Depending on the date of approval of the original application, you may be required to submit a 180-day report shortly after receipt of this letter.

Your 180-day reports must include the information listed in 21 CFR 601.70(b). FDA recommends that you use FORM FDA 3989, *PMR/PMC Annual Status Report for Drugs and Biologics,* to submit your 180-day reports.[4]

180-day reports must be clearly designated "**BLA 761263/S-006 180-Day AA PMR Progress Report**."

FDA will consider the submission of your application's ASR under section 506B(a)(1) and 21 CFR 601.70, in addition to the submission of reports 180 days after the date of approval of the original BLA each year (subject to a 60-day grace period), to satisfy the periodic reporting requirement under section 506B(a)(2).

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

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.

[3] You are required to submit information related to your confirmatory trial as part of your annual reporting requirement under section 506B(a)(1) until the FDA notifies you, in writing, that the Agency concurs that the study requirement has been fulfilled or that the study either is no longer feasible or would no longer provide useful information.

[4] FORM FDA 3989, along with instructions for completing this form, is available on the FDA Forms web page at https://www.fda.gov/about-fda/reports-manuals-forms/forms.

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*.[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 Kimberly Scott, Regulatory Project Manager, at 240-402-4560 or via email at Kimberly.Scott@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

[5] https://www.fda.gov/media/128163/download

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/

NICOLE J GORMLEY
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