CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

761430Orig1s000

Trade Name:	IMAAVY injection, for intravenous use
Generic or Proper Name:	(nipocalimab-aahu)
Sponsor:	Janssen Biotech, Inc.
Approval Date:	April 29, 2025
Indication:	IMAAVY is a neonatal Fc receptor (FcRn) blocker indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or antimuscle-specific tyrosine kinase (MuSK) antibody positive.

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CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	**X**
REMS	
Officer/Employee List	**X**
Integrated Review(s)	**X**
Product Quality Review(s)	**X**
Other Reviews	**X**
Risk Assessment and Risk Mitigation Review(s)	**X**
Proprietary Name Review(s)	**X**
Administrative/Correspondence Document(s)	**X**

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APPROVAL LETTER

BLA 761430

BLA APPROVAL

Janssen Biotech, Inc.
Attention: Beth Geter-Douglass, PhD
Director, Regulatory Affairs
1125 Trenton-Harbourton Road
Titusville, NJ 08560

Dear Dr. Geter-Douglass:

Please refer to your biologics license application (BLA) received August 29, 2024, and your amendments, submitted under section 351(a) of the Public Health Service Act for Imaavy (nipocalimab-aahu) injection, for intravenous use.

LICENSING

We have approved your BLA for Imaavy (nipocalimab-aahu) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Imaavy under your existing Department of Health and Human Services U.S. License No. 1864. Imaavy is indicated for the treatment of generalized myasthenia gravis (gMG) in adult and pediatric patients 12 years of age and older who are anti-acetylcholine receptor (AChR) or anti-muscle-specific tyrosine kinase (MuSK) antibody positive.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture nipocalimab-aahu drug substance at WuXi Biologics Co., Ltd in Wuxi, China. The final formulated drug product will be manufactured and filled at Vetter Pharma-Fertigung GmbH & Co. KG, Ravensburg, Germany. The final drug product labeling and secondary packaging will be performed at Cilag AG, Schaffhausen, Switzerland. You may label your product with the proprietary name, Imaavy, and market it in 300 mg/1.62 mL and 1,200 mg/6.5 mL single-dose vial, injection.

DATING PERIOD

The dating period for Imaavy shall be 18 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 drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4)

Results of ongoing stability studies 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 protocol(s) in your license application for the purpose of extending the expiration dating period of your 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 Imaavy 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 Imaavy, 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.

[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.

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the carton labeling submitted on February 25, 2025, and container labels submitted on April 7, 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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761430**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for nipocalimab was not referred to an FDA advisory committee because this biologic is not the first in its class.

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 REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of adverse maternal, fetal, and infant outcomes resulting from exposure to Imaavy during pregnancy and an unexpected serious risk of the potential presence of nipocalimab in human breast milk resulting in effects on the breastfed infant.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4833-1 Conduct a worldwide descriptive study that collects prospective and retrospective data in women exposed to Imaavy (nipocalimab) during pregnancy and lactation to assess risk of pregnancy and maternal complications, adverse effects on the developing fetus and neonate, and adverse effects on the infant. Infant outcomes will be assessed through at least the first year of life. The minimum number of patients will be specified in the protocol. The protocol must be agreed upon with the Agency.

The timetable you submitted on April 16, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2025
Final Protocol Submission:	04/2026
Interim Reports:	04/2029
	04/2033
	04/2035
Study Completion:	04/2036
Final Report Submission:	10/2036

4833-2 Perform a lactation study (milk only or mother/infant pair study) in lactating women who have received therapeutic doses of Imaavy using a validated assay to assess concentrations of nipocalimab in breast milk and to assess the effects on the breastfed infant, if available, based on study population.

The timetable you submitted on April 16, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2025
Final Protocol Submission:	04/2026
Study Completion:	04/2027
Final Report Submission:	10/2027

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.[3]

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Submit clinical protocol(s) to your IND 138975 with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o), REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

Submission of the protocol(s) for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70 . We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

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

We remind you of your postmarketing commitments:

4833-3	Perform a supplemental low endotoxin recovery (LER) study to examine the effects of hold time at (b) (4) on endotoxin recovery using 3 batches of each nipocalimab drug product presentation spiked with Reference Standard Endotoxin (RSE), or Control Standard Endotoxin (CSE) that is fully susceptible to LER and investigate additional endotoxin detection methods if LER is shown.

The timetable you submitted on April 18, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2025

Submit clinical protocols to your IND 138975 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*.[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We request that for Imaavy you submit all serious and non-serious cases of thromboembolic events; as well as all serious cases of malignancy, reactivation of hepatitis B or of latent tuberculosis, and infection, including opportunistic infection, as 15-day "Alert reports" (described under 21 CFR 600.80(c)(1)) through the 5th year following initial U.S. approval.

We request that you provide a narrative summary of the above events, including analyses of thromboembolic events; malignancy; reactivation of hepatitis B or of latent tuberculosis; and infection, including opportunistic infection as part of your required periodic safety reports [e.g., periodic adverse drug experience report (PADER) required under 21 CFR 600.80(c)(2) through the 5th year following initial U.S. approval date.

Your analyses should include interval and cumulative data relative to the date of approval of Imaavy. Your analyses should provide an assessment of causality, with documentation of risk factors and results of all assessments that support the diagnosis or the causality, including IgG levels if available, along with extent of exposure to Imaavy, indication, temporal association, duration of therapy, associated signs and symptoms, confounders, treatment given for the event, outcome, and dechallenge/rechallenge.

We also request that, in the narrative portion of your required periodic safety reports, you submit annual reports of Imaavy utilization rates and patient exposure, including quantity of doses or units (vials, prefilled syringes, etc.) administered to patients,

calculated cumulatively from the initial U.S. approval date annually through the 5th year following the initial U.S. approval date.

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, call the Regulatory Project Manager for this application.

If you have any questions, contact Jemini Patel, Regulatory Project Manager, at jemini.patel@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Teresa Buracchio, MD
Director
Office of Neuroscience
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert

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/

TERESA J BURACCHIO
04/29/2025 03:04:23 PM