BLA 761152

BLA APPROVAL

Omeros Corporation
Attention: Catherine A. Melfi, Ph.D.
Chief Regulatory Officer
201 Elliott Avenue West
Seattle, WA 98119

Dear Dr. Melfi:

Please refer to your biologics license application (BLA) received November 17, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Yartemlea (narsoplimab-wuug) injection.

We acknowledge receipt of your resubmission dated March 26, 2025, which constituted a complete response to our October 15, 2021, action letter.

We acknowledge receipt of your major amendments dated May 20, 2025, and May 27, 2025, which extended the goal date by three months.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2141 to Omeros Corporation, Seattle, WA, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Yartemlea (narsoplimab-wuug). Yartemlea is indicated for the treatment of adult and pediatric patients two years of age and older with hematopoietic stem cell transplant-associated thrombotic microangiopathy (TA-TMA).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture narsoplimab-wuug drug substance at Lonza Biologics Tuas Pte. Ltd. in Singapore, Singapore. The final formulated drug product will be manufactured and filled at Vetter Pharma-Fertigung GmbH & Co. KG, Langenargen, Germany. The filled drug product will be labeled and packaged at (b) (4) You may label your product with the proprietary name, Yartemlea, and market it in 370 mg/2 mL solution.

DATING PERIOD

The dating period for Yartemlea shall be 48 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) °C.

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 in your license application for the purpose of extending the expiration dating period of your drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Yartemlea 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 Yartemlea, 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). 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]

[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

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 761152**." Approval of this submission by FDA is not required before the labeling is used.

RARE PEDIATRIC DISEASE PRIORITY REVIEW VOUCHER

We also inform you that your request for a rare pediatric disease priority review voucher (RPD PRV) is denied. After the original enactment of section 529 of the Federal Food, Drug, and Cosmetic Act (FD&C Act),[3] in the Advancing Hope Act of 2016,[4] Congress created a requirement for sponsors seeking an RPD PRV to notify FDA of an intent to request an RPD PRV "upon submission" of the application that is the basis of the request. Specifically, section 529(b)(4)(A)(i) of the FD&C Act provides: "Beginning on the date that is 90 days after the date of enactment of the Advancing Hope Act of 2016, the sponsor of a rare pediatric disease product application that intends to request a priority review voucher under this section shall notify the Secretary of such intent upon submission of the rare pediatric disease product application that is the basis of the request for a priority review voucher." When you submitted your original BLA 761152 on November 17, 2020, you did not notify FDA of your intent to request an RPD PRV. It was not until approximately five years later, on November 2, 2025, that you submitted an amendment to BLA 761152 requesting an RPD PRV. You have not satisfied the requirement in section 529(b)(4)(A)(i) of the FD&C Act to notify FDA of an intent to request an RPD PRV "upon submission" of a potential rare pediatric disease product application.[5]

Additionally, under the current provisions in the law, as amended by the Continuing Appropriations and Extensions Act, 2025,[6] the RPD PRV program began to sunset after December 20, 2024. Section 529(b)(5) of the FD&C Act states:

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[3] Section 908 of the Food and Drug Administration Safety and Innovation Act (FDASIA), enacted on July 9, 2012, added section 529 to the FD&C Act. See Pub. L. No. 112-144.

[4] Pub. L. No. 114-229 (September 30, 2016).

[5] Because the Agency has determined that BLA 761152 is not eligible for an RPD PRV for the reasons stated in this letter, we have not needed to determine whether BLA 761152 meets other aspects of the RPD PRV eligibility criteria, including whether BLA 761152 qualifies as a "rare pediatric disease product application" under section 529(a)(4) of the FD&C Act.

[6] Pub. L. No. 118-83 (September 26, 2024).

> The Secretary may not award any priority review vouchers […] after December 20, 2024, unless the rare pediatric disease product application—
>
> (A) is for a drug that, not later than December 20, 2024, is designated […] as a drug for a rare pediatric disease; and
>
> (B) is, not later than September 30, 2026, approved under section 505(b)(1) of this title or section 351(a) of the Public Health Service Act.

BLA 761152 is not for a drug that FDA designated as a drug for a rare pediatric disease by December 20, 2024.[7, 8] Thus, as of the date of this letter, FDA "may not award [a] priority review voucher[]" under section 529 of the FD&C Act for BLA 761152.

For these reasons, the Agency has determined that you have not satisfied the notification requirement in section 529(b)(4)(A)(i) of the FD&C Act and that, in accordance with section 529(b)(5) of the FD&C Act, FDA may not award an RPD PRV for BLA 761152. Accordingly, your request for an RPD PRV is denied.

ADVISORY COMMITTEE

Your application for narsoplimab-wuug was not referred to an FDA advisory committee because outside expertise was not necessary.

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

[7] See section 529(b)(5) of the FD&C Act.

[8] Section 529(d)(2) of the FD&C Act provides that "requesting [RPD] designation under this subsection is not a prerequisite to receiving a priority review voucher under this section." However, by operation of the current termination of authority provision in section 529(b)(5) of the FD&C Act, FDA "may not award any [RPD] priority review voucher[]" after December 20, 2024, unless "the rare pediatric disease product application," in relevant part, "is for a drug that, not later than December 20, 2024, is designated [. . .] as a drug for a rare pediatric disease."

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 assess a known serious risk of serious infections.

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 this serious risk.

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

4938-1 Establish a registry to characterize the long-term safety of narsoplimab-wuug in at least 50 adult and pediatric patients with transplant-associated thrombotic microangiopathy (TA-TMA), with at least 1 year of follow-up. The final study report should include a summary of the major safety findings for all patients including patient level data on narsoplimab-wuug dosing, serious infections, serious treatment emergent adverse events and laboratory data (i.e., CBC with differential and renal function tests), autoimmune disorders, concomitant medications, vital status, and cause of death for any fatalities.

The timetable you submitted on December 12, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 06/2026
Final Protocol Submission: 12/2026
Study/Trial Completion: 12/2033
Final Report Submission: 12/2034

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.[9]

Submit clinical protocol(s) to your IND 120524 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).**

[9] 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.

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 SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4938-2 Provide safety, pharmacokinetic (PK) and pharmacodynamic (PD) data in pediatric patients <17 years of age treated with the recommended dosing regimen of narsoplimab for transplant-associated thrombotic microangiopathy (TA-TMA).

The timetable you submitted on November 26, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 06/2026
Final Protocol Submission: 12/2026
Study/Trial Completion: 12/2032
Final Report Submission: 12/2033

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

We remind you of your postmarketing commitments:

4938-3 Conduct a worst-case in-use stability study to evaluate the suitability of preparation and administration conditions for narsoplimab under clinically relevant conditions. The study should assess product stability under stressed conditions including but not limited to extended light exposure as mechanical stress from mixing as well as worst-case dilutions and volumes. All incompatibilities should be investigated to inform the labeling. Propose revisions to the labeling as appropriate.

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

Final Report Submission: 10/2026

4938-4 Perform a reproducibility evaluation for size exclusion chromatography (SEC), cation exchange chromatography (CEX), and capillary electrophoresis (CE-SDS) reduced and nonreduced with appropriate stressed stability samples to support Vetter as a quality control testing site for narsoplimab stability samples.

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

Final Report Submission: 10/2026

4938-5 Establish an appropriately justified drug product stability specification for (b) (4) based on levels observed in clinical and commercial batches

The timetable you submitted on October 23, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/2026

4938-6 Complete the pending real-world shipping study for drug product transportation from the drug product manufacturing site to the drug product packaging and labeling facility. Perform an additional real-world shipping study for drug product transportation from the drug product packaging and labeling facility to distribution centers and/or storage warehouses. This study will be performed using representative commercial drug product lots under commercial shipping conditions and will include a total of three shipments, and the evaluation will include assessments for shipping temperature, integrity of the vials and/or packaging/labeling as well as product quality attributes from samples collected prior to and after shipment.

The timetable you submitted on October 28, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2026

4938-7 Conduct narsoplimab container closure integrity test (CCIT) validation with the (b) (4) container closure system used for the narsoplimab drug product, including assessments of sensitivity, intermediate precision, and robustness.

The timetable you submitted on November 12, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2026

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 120524 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*.[10]

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.[11] Information and Instructions for completing the form can be found at FDA.gov.[12]

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

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

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, call the Regulatory Project Manager for this application.

If you have any questions, contact May Zuwannin, Regulatory Project Manager, at 301-796-7775 or May.Zuwannin@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Lisa Yanoff, MD
Deputy Director
Office of Cardiology, Hematology,
Endocrinology, and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
- 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/

LISA B YANOFF
12/23/2025 05:00:43 PM