U.S. FOOD & DRUG ADMINISTRATION

Our STN: BL 125856/0

**BLA APPROVAL**
November 24, 2025

Novartis Gene Therapies, Inc.
Attention: Lisa Krueger, PharmD
2275 Half Day Road, Suite 300
Bannockburn, IL 60015

Dear Dr. Krueger:

Please refer to your Biologics License Application (BLA) received March 28, 2025, submitted under section 351(a) of the Public Health Service Act (PHS Act) for onasemnogene abeparvovec-brve.

## LICENSING

We have approved your BLA for onasemnogene abeparvovec-brve effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, onasemnogene abeparvovec-brve under your existing Department of Health and Human Services U.S. License No. 2250. Onasemnogene abeparvovec-brve is indicated for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients 2 years of age and older with confirmed mutation in *survival motor neuron 1 (SMN1)* gene.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 03381729, 03421977, 04042025, 05089656, 05335876, 05386680.

## MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture onasemnogene abeparvovec-brve at your facility located at Novartis Gene Therapies, Inc. in (b) (4) You may label your product with the proprietary name ITVISMA and market it in single-dose vials containing 3 mL product.

## ADVISORY COMMITTEE

We did not refer your application to the Cellular, Tissue, and Gene Therapies Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

## DATING PERIOD

The dating period for onasemnogene abeparvovec-brve drug product shall be 24 months from the date of manufacture when stored upright at ≤-60°C. The date of manufacture shall be defined as the date on which the last vial of the drug product is sealed. Following the (b) (4) sterile filtration, (b) (4) is allowed, (b) (4) (b) (4) under limited conditions (failure of the (b) (4) sterile filter (b) (4) loss of integrity of the (b) (4) the filtered drug product and the filling needle, and setup issues associated with the filling needle assembly not caused by operator error). The dating period for your drug substance shall be (b) (4) when stored at (b) (4)

## FDA LOT RELEASE

Please submit protocols showing results of all applicable tests. You may not distribute any lots of products until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

## BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, 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 the Director, Office of Compliance and Biologics Quality, electronically through the eBPDR web application or at the address below. Links for the instructions on completing the electronic form (eBPDR) may be found on CBER's web site at https://www.fda.gov/vaccines-blood-biologics/report-problem-center-biologics-evaluation-research/biological-product-deviations :

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

## MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of onasemnogene abeparvovec-brve, or in the manufacturing facilities.

## LABELING

We hereby approve the draft content of labeling including the Package Insert submitted under amendment 47, dated November 20, 2025 and the draft package and container labels submitted under amendment 43, dated November 17, 2025.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on November 20, 2025. 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* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels identical to the package and container labels submitted on November 17, 2025, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm333969.pdf.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125856/0 at the time of use and include implementation information on Form FDA 356h.

## ADVERTISING AND PROMOTIONAL LABELING

You may submit proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
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10903 New Hampshire Ave.
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You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

**ADVERSE EVENT REPORTING**

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. In addition to the reporting requirements in 21 CFR 600.80, you must submit adverse experience reports for cases of hepatic failure, thrombotic microangiopathy, and peripheral sensory neuropathy as 15-day expedited reports to the FDA Adverse Event Reporting System (FAERS). Hepatic failure, thrombotic microangiopathy, and peripheral sensory neuropathy reports must be submitted as 15-day expedited reports for three years following the date of product licensure. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format — Postmarketing Safety Reports* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports and FDA's Adverse Event reporting System website at https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at https://www.fda.gov/vaccines-blood-biologics/lot-release/lot-distribution-database-ldd.

**RARE PEDIATRIC DISEASE PRIORITY REVIEW VOUCHER**

Your request for a rare pediatric disease priority review voucher has been denied. You did not qualify for the voucher because your application did not meet the requirements to be a "rare pediatric disease product application" under section 529(a)(4) of the Federal Food, Drug & Cosmetic Act (FD&C Act). FDA has determined that BLA 125856 is not a human drug application for a biological product that contains no active ingredient that has been previously approved in any other application under section 351(a) or 351(k) of the PHS Act. Specifically, BLA 125856 is for a biological product that contains an active ingredient that was previously approved in another application under section 351(a) of the PHS Act. The active ingredient onasemnogene abeparvovec was previously approved on May 24, 2019, in BLA 125694 for ZOLGENSMA.

**PEDIATRIC REQUIREMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because the biological product for this indication has an orphan drug designation, you are exempt from this requirement.

The biological product was studied in the pediatric patients 2 years of age or older for the intended indication.

**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, please contact the Regulatory Project Manager for this application.

Sincerely,

Asha Das, MD
Acting Director
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research