Our STN: BL 125781/0

ACCELERATED BLA APPROVAL
June 22, 2023

Sarepta Therapeutics, Inc.
Attention: Patrick O'Malley
215 First Street
Cambridge, MA 02142

Dear Mr. O'Malley:

Please refer to your Biologics License Application (BLA) received September 28, 2022, under section 351(a) of the Public Health Service Act (PHS Act) for delandistrogene moxeparvovec-rokl.

LICENSING

We are issuing Department of Health and Human Services U.S. License No. 2308 to Sarepta Therapeutics, Inc., Cambridge, MA, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products and pursuant to section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) and the regulations for accelerated approval, 21 CFR 601.41. 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 delandistrogene moxeparvovec-rokl. Delandistrogene moxeparvovec-rokl is indicated for treatment of ambulatory pediatric patients aged 4 through 5 years with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: NCT03375164, NCT03769116, and NCT04626674.

ACCELERATED APPROVAL REQUIREMENTS

Under accelerated approval statutory provisions and regulations, we may grant marketing approval for a biological product on the basis of adequate and well-controlled clinical trials establishing that the biological product has an effect on a surrogate endpoint that is reasonably likely, based on epidemiologic, therapeutic, pathophysiologic, or other evidence, to predict clinical benefit, or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity that is reasonably likely to predict survival or irreversible morbidity. This approval requires you

to study the biological product further, to verify and describe its clinical benefit, where there is uncertainty as to the relation of the surrogate endpoint to clinical benefit, or of the observed clinical benefit to ultimate outcome.

Approval under these statutory provisions and regulations requires, among other things, that you conduct adequate and well-controlled clinical trials to verify and describe clinical benefit attributable to this product. Clinical benefit is evidenced by effects such as improved North Star Ambulatory Assessment (NSAA) Total Score from baseline to Week 52 after treatment with delandistrogene moxeparvovec-rokl when compared with an appropriate concurrent control group.

Accelerated Approval Required Studies

We remind you of your postmarketing requirement specified in your submission of June 6, 2023.

1. Complete Study SRP-9001-301 Part 1, an ongoing, randomized, double-blinded clinical trial intended to describe and verify clinical benefit of delandistrogene moxeparvovec-rokl in ambulatory patients with Duchenne muscular dystrophy (DMD). The trial evaluates the primary endpoint of North Star Ambulatory Assessment (NSAA) and compares delandistrogene moxeparvovec-rokl to placebo in 125 ambulatory patients with DMD with confirmed mutation in the *DMD* gene.

   Final Protocol Submission: Submitted

   Trial Completion: September 30, 2023

   Final Report Submission: January 31, 2024

We expect you to complete and report this trial within the framework described in your letter of June 6, 2023.

We acknowledge that you have provided the final protocol to your IND 17763. Please provide a letter of cross-reference to this BLA, STN BL 125781, explaining that this protocol was submitted to the IND. Please refer to the sequential number for each trial and the submission number as shown in this letter.

You must conduct this trial with due diligence. If this required postmarketing trial fails to verify that clinical benefit is conferred by delandistrogene moxeparvovec-rokl or is not conducted with due diligence, including with respect to the conditions set forth below, we may withdraw this approval.

You must submit reports of the progress of each trial required under section 506(c) of the FDCA to this BLA 180 days after the date of approval of this BLA and every 180

days thereafter as required under section 506B(a)(2) of the FDCA. The submission of these reports will be subject to a 60-day grace period.

The reports should include:

- expected trial completion and final report submission dates
- any changes in plans since the last report, with rationale for any changes,
- the current number of patients entered into each trial.

Reports submitted 180 days after the date of approval of this BLA, subject to a 60-day grace period, and on such date each year thereafter must be labeled **180-Day AA PMR Progress Report**.

Reports submitted one year after the date of approval of this BLA and on such date each year thereafter may be submitted as part of your annual status report required under section 506B(a)(1) of the FDCA and 21 CFR 601.70. FDA will consider the submission of your annual status report under section 506B(a)(1) and 21 CFR 601.70, in addition to the submission of progress reports 180 days after the date of approval and on such date each year thereafter, to satisfy the periodic reporting requirement under section 506B(a)(2).

Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Postmarketing Requirements and 506B Commitments are fulfilled or released.

Please submit a final study report as a supplement to this BLA, STN BL 125781. For administrative purposes, all submissions related to this postmarketing study requirement must be clearly designated as "**Subpart E Postmarketing Study Requirements.**"

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture delandistrogene moxeparvovec-rokl drug substance at Catalent Pharma Services, Catalent Maryland (BWI), 7555 Harmans Road, Harmans, MD 20177, USA. The final formulated drug product will be manufactured at Catalent Pharma Solutions, Catalent Maryland (Biopark), 801 West Baltimore Street, Suite 302, Baltimore, MD 21201, USA; and labeled and packaged at the (b) (4)

You may label your product with the proprietary name ELEVIDYS and market it in 10 mL vials.

DATING PERIOD

The dating period for delandistrogene moxeparvovec-rokl shall be 12 months from the date of manufacture when stored at ≤ -60°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. Following the final sterile filtration, no reprocessing/reworking is allowed without prior approval from the Agency. The dating period for your drug substance shall be (b) (4) when stored at (b) (4). We have approved the stability protocols 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

Please submit protocols showing results of all applicable tests. You may not distribute any lots of product 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 delandistrogene moxeparvovec-rokl, or in the manufacturing facilities.

LABELING

We hereby approve the draft content of labeling including the Package Insert submitted under amendment 76, dated June 21, 2023, and the draft carton and container labels submitted under amendments 70 and 77, dated June 15, 2023 and June 21, 2023.

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 June 21, 2023. 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.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on June 15, 2023 and June 21, 2023, 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/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125781 at the time of use and include implementation information on Form FDA 356h.

PROMOTIONAL MATERIALS

Please note that the accelerated approval regulation concerning promotional materials (21 CFR 601.45) stipulates that all advertising and promotional labeling items that you wish to distribute in the first 120 days following approval, must have been received by FDA prior to the approval date. After approval, promotional items intended for dissemination after the first 120 days following approval must be submitted to the FDA at least 30 days prior to the anticipated distribution date. Please submit draft materials with a cover letter noting that the items are for accelerated approval, and an accompanying FORM FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

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

You must submit copies of your final advertisement and promotional labeling at the time of initial dissemination or publication, accompanied by FORM FDA 2253 (21 CFR 601.12(f)(4)).

Alternatively, you may submit promotional materials for accelerated approval products electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs* at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf.

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 acute liver injury, immune-mediated myositis, myocarditis, and thrombotic microangiopathy as 15-day expedited reports (regardless of seriousness or expectedness) to the FDA Adverse Event Reporting System (FAERS). Acute liver injury, immune-mediated myositis, myocarditis, and thrombotic microangiopathy reports must be submitted as 15-day expedited reports for 3 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072369 and FDA's Adverse Event reporting System website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm.

RARE PEDIATRIC DISEASE PRIORITY REVIEW VOUCHER

We also inform you that you have been granted a rare pediatric disease priority review voucher (PRV), as provided under section 529 of the FDCA. This PRV has been assigned a tracking number, PRV BLA 125781. All correspondences related to this voucher should refer to this tracking number.

This voucher entitles you to designate a single human drug application submitted under section 505(b)(1) of the FDCA or a single biologic application submitted under section 351 of the Public Health Service Act as qualifying for a priority review. Such an application would not have to meet any other requirements for a priority review. The list below describes the sponsor responsibilities and the parameters for using and transferring a rare pediatric disease priority review voucher.

- The sponsor who redeems the PRV must notify FDA of its intent to submit an application with a PRV at least 90 days before submission of the application and must include the date the sponsor intends to submit the application. This notification should be prominently marked, "**Notification of Intent to Submit an Application with a Rare Pediatric Disease Priority Review Voucher**."
- This PRV may be transferred, including by sale, by you to another sponsor of a human drug or biologic application. There is no limit on the number of times that the PRV may be transferred, but each person to whom the PRV is transferred must notify FDA of the change in ownership of the voucher not later than 30 days after the transfer. If you retain and redeem this PRV, you should refer to this letter as an official record of the voucher. If the PRV is transferred, the sponsor to whom the PRV has been transferred should include a copy of this letter (which will be posted on our website as are all approval letters) and proof that the PRV was transferred.
- FDA may revoke the PRV if the rare pediatric disease product for which the PRV was awarded is not marketed in the U.S. within 1 year following the date of approval.
- The sponsor of an approved rare pediatric disease product application who is awarded a PRV must submit a report to FDA no later than 5 years after approval that addresses, for each of the first 4 post-approval years:
    - the estimated population in the U.S. suffering from the rare pediatric disease for which the product was approved (both the entire population and the population aged 0 through 18 years),
    - the estimated demand in the U.S. for the product, and
    - the actual amount of product distributed in the U.S.

You may also review the requirements related to this program by visiting FDA's Rare Pediatric Disease PRV Program webpage available at https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm.

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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We acknowledge your written commitment as described in your submission of June 22, 2023, as outlined below:

2. Sarepta commits to conducting adequate analytical and clinical validation testing to establish an (b) (4) that can be used to identify patients with DMD who may benefit from delandistrogene moxeparvovec-rokl therapy. The results of the validation study are intended to inform product labeling. The clinical validation should be supported by a clinical bridging study comparing the in (b) (4) and the clinical trial enrollment assays.

   (b) (4)

The PMC will be considered fulfilled (b) (4)

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;

- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

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

We acknowledge your written commitments as described in your submission of May 30, 2023, and June 8, 2023, as outlined below:

3. Sarepta Therapeutics, Inc. commits to performing (b) (4) as a "Postmarketing Commitment - Final Study Report" by July 31, 2024.

   Final Report Submission: July 31, 2024

4. Sarepta Therapeutics, Inc. commits to submitting a final report for the supplemental (b) (4) manufacturing runs for (b) (4) at the Catalent facility as a "Postmarketing Commitment - Final Study Report" by June 30, 2024.

   Final Report Submission: June 30, 2024

5. Sarepta Therapeutics, Inc. commits to submitting a final report of the (b) (4) as a "Postmarketing Commitment - Final Study Report" by March 31, 2024.

   Final Report Submission: March 31, 2024

6. Sarepta Therapeutics, Inc. commits to revising the system suitability criteria set in the SOP for (b) (4) to reflect the assay variability (percent coefficient of variation; %CV) observed in intermediate precision during assay validation and to submitting the revised SOP as a "Postmarketing Commitment - Final Study Report" by December 31, 2023.

   Final Report Submission: December 31, 2023

7. Sarepta Therapeutics, Inc. commits to revising the system suitability in the SOP for the in (b) (4) assay to include a parameter determining (b) (4)

and to submitting the revised SOP as a "Postmarketing Commitment – Final Study Report" by June 30, 2024.

Final Report Submission: June 30, 2024

8. Sarepta Therapeutics, Inc. commits to reassessing the commercial acceptance criterion for the release testing of potency of SRP-9001 drug product after data have been collected on (b) (4) commercial lots and submit a "Postmarketing Commitment – Final Study Report" by June 30, 2024.

   Final Report Submission: June 30, 2024

9. Sarepta Therapeutics, Inc. commits to implementing the following CMC change for the SRP-9001 (b) (4) The CMC change will be submitted as a "Postmarketing Commitment - Final Study Report" by December 31, 2024.

   Final Report Submission: December 31, 2024

10. Sarepta Therapeutics, Inc. commits to performing (b) (4) . The final report will be submitted as a "Postmarketing Commitment – Final Study Report" by December 31, 2024.

    Final Report Submission: December 31, 2024

We request that you submit information concerning chemistry, manufacturing, and control postmarketing commitments and final reports to this BLA, STN BL 125781. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Study**

Commitment – Correspondence Status Update. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment Final Study Report**.

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,

Melissa Mendoza, JD
Director
Office of Compliance
and Biologics Quality
Center for Biologics
Evaluation and Research

Peter Marks, MD, PhD
Director
Center for Biologics
Evaluation and Research