Our STN: BL 125781/34

SUPPLEMENT APPROVAL
PMR FULFILLED
SUPPLEMENT ACCELERATED APPROVAL
June 20, 2024

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

Dear Patrick O'Malley:

We have approved your request received December 21, 2023, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act (PHS Act) for delandistrogene moxeparvovec-rokl to expand the approved indication to individuals at least 4 years of age for the treatment of Duchenne muscular dystrophy (DMD) in patients who are ambulatory and have a confirmed mutation in the *DMD* gene.

We have also approved your request to supplement your BLA submitted under section 351(a) of the PHS Act for delandistrogene moxeparvovec-rokl to expand the approved indication to individuals at least 4 years of age for the treatment of DMD in patients who are non-ambulatory and have a confirmed mutation in the *DMD* gene, according to the regulations for accelerated approval, 21 CFR 601.41. The DMD indication in non-ambulatory patients is approved under accelerated approval based on expression of ELEVIDYS micro-dystrophin.

The review of this supplement was associated with the following National Clinical Trial (NCT) numbers: NCT05096221 and NCT04626674.

ACCELERATED APPROVAL REQUIREMENTS

Under accelerated approval regulations statutory provisions and 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. 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.

ACCELERATED APPROVAL REQUIRED STUDIES

We remind you of your postmarketing requirement (PMR) specified in your submission of June 11, 2024.

1. Conduct and submit the results of a randomized, controlled trial to verify and confirm the clinical benefit of delandistrogene moxeparvovec-rokl in patients with Duchenne's muscular dystrophy, who are non-ambulatory and have a confirmed mutation in the DMD gene. The trial should evaluate the effects of delandistrogene moxeparvovec-rokl on an endpoint that denotes clinical benefit.

   Final Protocol Submission: Submitted

   Study/Trial Completion: May 30, 2027

   Final Report Submission: November 30, 2027

We expect you to complete design, initiation, accrual, completion, and reporting of these studies within the framework described in your letter of June 11, 2024.

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 required postmarketing trial(s) fail to verify that clinical benefit is conferred by delandistrogene moxeparvovec-rokl, or are 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 listed above as required under section 506(c) of the Federal Food, Drug, and Cosmetic Act (FDCA) to this BLA 180 days after the date of approval of this BLA and approximately every 180 days thereafter (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 506(c) of the FDCA. The initial report will be a standalone submission and the subsequent report will be combined with your application's annual status report 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. Submit the subsequent 180-day report with your application's annual status report. Submit both of

these 180-day reports each year until the final report for the corresponding study or clinical trial is submitted.

Your 180-day report 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. 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.

Your 180-day reports, including both the standalone 180-day report submitted 180 days after the date of approval and the 180-day report submitted with your annual status report, must be clearly designated as **180-Day AA PMR Progress Report.**

FDA will consider the submission of your annual status report under section 506B(a)(1) of the FDCA and 21 CFR 601.70, in addition to the submission of reports 180 days after the date of approval each year, to satisfy the periodic reporting requirement under section 506B(a)(2) of the FDCA. You are also required to submit information related to your confirmatory trial as part of your annual reporting requirement under section 506B(a)(1) of the FDCA 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.

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 your original BLA until all Postmarketing Requirements and 506B Commitments are fulfilled or released.

Please submit the 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**."

FULFILLED ACCELERATED APPROVAL REQUIRED STUDIES

We approved BLA STN BL 125781/0 on June 22, 2023, under 21 CFR 601 Subpart E for Accelerated Approval of Biological Products for Serious or Life-Threatening Illnesses. Approval of this supplement fulfills the following postmarketing requirement for 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) made under 21 CFR 601.41.

STN: BL 125781/0

PMR #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: September 8, 2021

Study/Trial Completion: September 13, 2023

Final Report Submission: January 11, 2024

LABELING

We hereby approve the draft content of labeling Package Insert submitted under amendment 21, dated June 17, 2024.

WAIVER OF HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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 17, 2024. 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.

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.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the 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
Document Control Center
10903 New Hampshire Ave.
WO71–G112
Silver Spring, MD 20993-0002

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)).

For each pending supplemental application for this BLA that includes proposed revised labeling, please submit an amendment to update the proposed revised labeling with the changes approved today.

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 available at

http://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)).

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.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

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