



Our STN: BL 125781/0

**MID-CYCLE COMMUNICATION
SUMMARY**
February 23, 2023

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

Dear Mr. O'Malley:

Attached is a copy of the summary of your January 24, 2023, Mid-Cycle Communication Teleconference with CBER. This memorandum constitutes the official record of the Teleconference. If your understanding of the Teleconference outcomes differs from those expressed in this summary, it is your responsibility to communicate with CBER as soon as possible.

Please include a reference to STN BL 125781/0 in your future submissions related to the subject product.

If you have any questions, please contact Rachel Duddy at Rachel.Duddy@fda.hhs.gov.

Sincerely,

Heather Lombardi, PhD
Director
Division of Cellular and Gene Therapies
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research

Mid-Cycle Communication Teleconference Summary

Application Type and Number: BLA 125781/0
Product Name: delandistrogene moxeparvovec
Proposed Indication for Use: Treatment of ambulatory patients with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the *DMD* gene
Applicant: Sarepta Therapeutics, Inc.
Meeting Date & Time: January 24, 2023, from 1:00pm- 2:00pm ET
Committee Chair: Emmanuel Adu-Gyamfi, PhD
RPM: Rachel Duddy, MS

Attendees:

Emmanuel Adu-Gyamfi, PhD, OTAT/DCGT
Meghna Alimchandani, MD, CBER/OBE
Atul Bhattaram, CDER/OTS/OCP/DPM
Lilia Bi, PhD, CBER/OTAT/DCGT
Wilson W. Bryan, MD, CBER/OTAT
Dennis Cato, CBER/OCBQ/DIS/BMB
Theresa Chen, PhD, OTAT/DCEPT
Benjamin Cyge, CBER/OCBQ/DCM/APLB
Brendan Day, MD, MPH, CBER/OBPV/DPV/PB2
Maureen DeMar, BSN, RN, CBER/OCBQ/DMPQ/ARB
Rachel Duddy, MS, CBER/OTAT/DRPM
Varsha Garnepudi, PhD, CBER/OCBQ/DBSQC
Denise Gavin, PhD, CBER/OTAT/DCGT
Leila Hann, CBER/OTAT
Andrew Harmon, PhD, CBER/OTAT/DCGT
Christopher Jason, MD CBER/OBPV/DE/PB
George Kastanis, MS, CBER/OCBQ/DBSQC/QAB
Carolyn Laurencot, PhD, CBER/OTAT/DCGT
Wei Liang, PhD, CBER/OTAT
Heather Lombardi, PhD, CBER/OTAT/DCGT
Olivia Ou Ma, PhD, CBER/OCBQ/DMPQ/MRB2
Iris Marklein, PhD, CBER/OTAT/DCGT
Narayan Nair, MD, CBER/OBPV/DE
Tyree Newman, CBER/OTAT/DRPM
Steven Oh, PhD, CBER/OTAT/DCGT
Tao Pan, PhD, CBER/OCBQ/DBSQC
Tejashri Purohit-Sheth, MD, CBER/OTAT/DCEPT
Sandhya Sanduja, PhD, CBER/OTAT/DCEPT
Andrey Sarafanov, PhD, CBER/OTAT/DPPT/HB
Kimberly Schultz, PhD, OTAT/DCGT
John Scott, PhD, MA, CBER/OBPV/DB
Anurag Sharma, PhD, CBER/OTAT/DCGT
Vishnu Sharma, PhD, CDER/OTS/OCP/DPM

Rosa Sherafat-Kazemzadeh, MD, OTAT/DCEPT
Mike Singer, MD, PhD, CBER/OTAT/DCEPT/GMB2
Ramani Sista, PhD, CBER/OTAT/DRPM
Sukyoung Sohn, PhD, CBER/OTAT/DCGT
Lisa Stockbridge, PhD, CBER/OCBQ/DCM/APLB
Brian Stultz, MS, CBER/OTAT/DCGT
Takeesha Taylor-Bell, CDRH/OPEQ/OHTVII/DIHD/HB
Triet M Tran, PharmD, CBER/OCBQ/DIS/BMB
Lei Xu, MD, PhD, OTAT/DCEPT
Zhenzhen Xu, PhD, CBER/OBPV/DB
Cong Wang, PhD, CBER/OBPV/DB
Xiaofei Wang, PhD, CBER/OTAT/DCEPT
Nadia Whitt, CBER/OTAT/DRPM
Boguang Zhen, PhD, CBER/OBPV

Discussion Summary:

1. Any significant issues/major deficiencies, categorized by discipline, identified by the Review Committee to date.

Chemistry, Manufacturing and Controls

- a. Insufficient information was provided to assess the suitability of the SRP-9001 primary reference standard. There is missing information needed to evaluate the long-term stability and continuous use of the reference vector. We requested SRP-9001 reference standard information in an Information Request (IR) dated January 20, 2023. The team will review the Applicant's response when received.
- b. Insufficient information was provided to assess the adequacy of the validation study for the (b) (4) test used to measure strength (vector genomes/mL) of the drug product (DP), which is critical to administering the appropriate dose. The (b) (4) test has been validated at (b) (4) different testing sites with notable differences in the assay performance metrics. There are also discrepancies in the different standard operating procedures (SOPs) that should be resolved to ensure consistent measurement of DP strength, regardless of the testing site. Details of this deficiency have been communicated by IR dated January 20, 2023.
- c. The release criteria for (b) (4) DP are exceptionally wide for all non-compendial measures of product quality, including strength (vector genome/mL), purity and potency and do not reflect the historical manufacturing data. The CMC team has requested the refinement of these release specifications by IR dated January 20, 2023, to ensure consistency of future batches of the SRP-9001 drug product.

- d. The DS release specification and the DS stability study do not include a test for (b) (4). In the absence of a validated (b) (4) test, the assurance of (b) (4) of the bulk DS after long term storage cannot be fully verified. During clinical development, the SRP-9001 DS batches were purified and processed through to the DP stage without long-term storage. CMC has requested that the Applicant include (b) (4) testing for DS release and stability assessment by IR on January 20, 2023.
- e. Insufficient information was provided to assess leachables in the DP. This deficiency was communicated through IR on January 20, 2023.

The applicant stated that they will respond to the January 20, 2023 IR on February 3, 2023.

2. Information regarding major safety concerns.

At this time, we have not identified major safety concerns.

The applicant will be submitting the 120-day safety update on Friday, January 27, 2023.

3. Preliminary Review Committee thinking regarding a) risk management, b) the potential need for any post-marketing requirement(s) (PMRs), and c) the ability of adverse event reporting and CBER's Sentinel Program to provide sufficient information about product risk.

Review is ongoing. The need for a Risk Evaluation and Mitigation Strategy (REMS), PMR or PMC remains undetermined at this juncture.

4. Any information requests sent, and responses not received.

- a. Information Request dated January 20, 2023, regarding SRP-9001 reference standard information is due February 3, 2023.

5. Any new information requests to be communicated.

As our review continues, new information requests will be conveyed as needed.

Additional clinical and clinical pharmacology information request(s) will be sent.

6. Proposed date for the Late-Cycle meeting (LCM).

The LCM between you and the Review Committee is currently scheduled for March 13, 2023, from 9:30am – 11:00am ET. We intend to send the LCM meeting materials to you by March 3, 2023.

If these timelines change, we will communicate updates to you during the course of the review.

7. Updates regarding plans for the AC meeting.

There is no Advisory Committee meeting currently planned for this application.

8. Other projected milestone dates for the remainder of the review cycle, including changes to previously communicated dates, and notification of intent to inspect manufacturing facilities.

Pre-license inspection (PLI) of the drug substance manufacturing facility located in Harmans, MD; drug product manufacturing facility located in Baltimore, MD; and the drug product testing site located in Andover, MA will be conducted. We will contact you regarding the scheduling of the PLI activities.

There are no changes to previously discussed dates. The late cycle meeting is scheduled for March 13, 2023, from 9:30am to 11:00am ET.

Tentative BIMO Target Date: March 20, 2023

Tentative Labeling Target Date: April 28, 2023

Tentative PMC Target Date: April 28, 2023