ENDURE: A Prospective, Observational Study of the Comparative Effectiveness and Safety of Delandistrogene Moxeparvovec in Routine Clinical Practice

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Background

- Delandistrogene moxeparvovec is an rAAVrh74 vector-based gene transfer therapy that delivers a transgene encoding delandistrogene moxeparvovec micro-dystrophin, an engineered, functional form of dystrophin shown to stabilize or slow disease progression in Duchenne muscular dystrophy (DMD)[1-4]
  - It is approved in the US and in other select countries[5-12]
- Existing data sources such as electronic health records or administrative claims are not suitable to adequately measure the impact of delandistrogene moxeparvovec on individuals' DMD disease progression and safety outcomes, particularly over long periods of time[13,14]
- Therefore, structured long-term follow-up in phase 4 studies provide important real-world treatment experience and data, that might not be captured outside of clinical trials, to inform decisions being made by families, clinicians, regulators, and payers

Objective

To describe the design of ENDURE (NCT06270719, SRP-9001-401), a study providing longitudinal follow-up on effectiveness and safety of delandistrogene moxeparvovec beyond the clinical trial setting and experience in a broad population of participants with DMD

Methods

- ENDURE aims to provide long-term effectiveness and safety data while:
  - Minimizing sources of bias through study design by reducing selection bias, recall bias, and measured and unmeasured confounding
  - Increasing comparability and generalizability to the real-word population
- To ensure comprehensive functional data collection, patient-reported outcomes (PRO) are collected using Patient-Reported Outcomes Measurement Information System (PROMIS), a set of PRO measures that evaluate physical, mental, and social health including fatigue, mobility, and upper extremity function
- Data outcomes collected aim to limit burden on patients, their caregivers, and their clinicians but still capture structured information on the treatment continuum
- To be consistent with standard of care and representative of the US DMD patient population, participation is not limited to delandistrogene moxeparvovec clinical trial sites
  - As of February 2025, there are 13 active sites in the US (**Figure 1**)

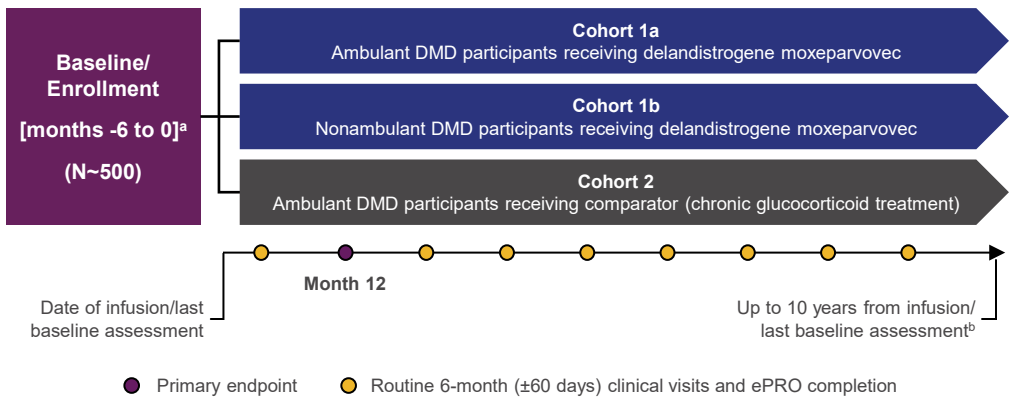
Figure 1 *ENDURE study centers*

Active site as of February 2025

Study Design[15]

- A phase 4, multicenter, prospective, observational study in participants aged ≥4 years (**Figure 2**)
- Medical history and prospective data on DMD treatment outcomes and safety are collected for up to 10 years from approximately 500 participants with DMD receiving either delandistrogene moxeparvovec or comparator therapy

Figure 2 *ENDURE study design*



[a]If >6 months between completion of baseline data collection and infusion of delandistrogene moxeparvovec, an additional baseline visit must be completed prior to infusion. [b]Or until censoring event including exposure to another DMD gene therapy, new participation in DMD clinical trial, death, disenrollment, loss to follow-up, 3,713 days of follow-up from baseline, or end of the study period.

Endpoints[15]

Primary endpoint

10-meter walk/run (MWR) at Month 12

Mean change from baseline in 10MWR (calculated velocity) at Month 12 among ambulant participants at baseline from Cohorts 1a and 2

Key secondary endpoints collected up to 10 years

FUNCTIONAL

- Time to rise from floor[a]
- 10MWR[a]
- Time to loss of ambulation (LOA)
- Performance of upper limb (PUL) version 2.0 entry item score[b]

SAFETY OUTCOMES

- Adverse events
- Safety outcomes of interest

PATIENT-REPORTED (PROMIS)

- Upper extremity
- Mobility[a]
- Fatigue[b]

CLINICAL

- Pulmonary: forced vital capacity (FVC), FVC% predicted
- Age at LOA
- Cardiac: left ventricular ejection fraction (LVEF) as measured by echocardiogram (ECHO)[b]

[a]Collected in baseline ambulant participants only. [b]Collected annually after first 12 months.

Eligibility Criteria

Inclusion criteria	Exclusion criteria
• Male ≥4 years old	• Deletion of the entirety or any portion of exon 8 and/or 9 in the *DMD* gene
• Clinical diagnosis of DMD and confirmed genetic testing	• Currently participating in any DMD interventional study
• Receiving or prescribed chronic glucocorticoid therapy	• Medical condition or confounding circumstances that, in the opinion of the investigator, might compromise with:
• **Cohort 1a:** Ambulant at screening	– Their ability to comply with the protocol-required procedures
• **Cohort 1b:** Nonambulant at screening	– Their well-being or safety
• **Cohort 2 comparators:** Ambulant participants unexposed to DMD gene therapy at screening	– The interpretation of the data collected

ENDURE

Key Findings

ENDURE is designed to collect follow-up data on participants who received delandistrogene moxeparvovec for up to 10 years post infusion, which will provide long-term effectiveness and safety compared with standard of care in a real-world setting

ENDURE began enrollment in the United States in February 2024

Abbreviations

10MWR=10-meter walk/run; DMD=Duchenne muscular dystrophy; ECHO=echocardiogram; ePRO=electronic patient-reported outcome; FVC=forced vital capacity; FVC%=percent forced vital capacity; LVEF=left ventricular ejection fraction; PRO=patient-reported outcome; PROMIS=Patient-Reported Outcomes Measurement Information System; PUL=performance of upper limb.

Acknowledgments & Disclosures

Acknowledgments: This study was funded by Sarepta Therapeutics, Inc. Editorial support was provided by Deborah Lew, PhD, of Eloquent Scientific Solutions and was funded by Sarepta Therapeutics, Inc.

Disclosures: All authors are employees of Sarepta Therapeutics, Inc., and may own stock/options in the company.

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Presented at Muscular Dystrophy Association 2025 Conference

March 16–19, 2025
Dallas, TX