Protocol C3391003

A PHASE 3, MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO EVALUATE THE SAFETY AND EFFICACY OF FORDADISTROGENE MOVAPARVOVEC (PF-06939926) FOR THE TREATMENT OF DUCHENNE MUSCULAR DYSTROPHY

Statistical Analysis Plan (SAP)

Version: 9 – Primary Analysis through Week 52

Date: 08-Apr-2024

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
9 08 Apr 2024	Amendment 15 28-Dec-2023	To clarify the timing of primary analysis based on protocol	Section 5 Added text "The primary analysis will occur after at least 90 FAS participants complete Day 360 (Visit 19) or discontinued from the study prior to Week 52 if they had received Year 1 IP at least one year prior to the data cutoff."
		Due to the transfer of the viral vector shedding assay to an internal lab during the course of the study and some differences in the results between the 2 assays, the analysis for endpoint viral vector levels are removed from the planned analysis as they may include data from both assays. switch of labs for the	Sections 6.3.8, Appendix 1 Removed analysis for viral vector levels endpoint
		To clarify the FAS definition for PCD analysis and align with protocol	Section 4 Changed the name of Full Analysis Set (FAS) to Full Analysis Set (FAS) (through Week 52) Added footnote to clarify the FAS for PCD analysis
		To evaluate the treatment effect more comprehensively using multiple endpoint	Sections 5.2.4, 6.4 Added global statistical test analysis for specified multiple functional endpoints
		To better present the analysis results	Sections 6.1.1, 6.2.2, 6.2.3, 6.2.4, 6.2.5, Appendix 1 Removed model-based summary of LS means at Week 52 for each age. Added standard error of each LS mean and estimated difference in LS mean in the summary Removed graph for Mean (SD) change from Baseline at Week 52 by age at the Screening visit.

		To update the ANCOVA analysis for biceps muscle biopsies by removing Baseline factor as the values at Baseline are expected to be around 0 and exhibit extremely low variability	Sections 6.2.1.1, 6.2.12, Appendix 1 Removed text "Baseline (continuous variable)" from the ANCOVA model
		To evaluate actigraphy endpoints based on statistical model and aid in the interpretation of the treatment effect	Section 5.4, 6.3.2, Appendix 1 Added clarification that mean will be calculated for visits with at least 4 compliant days Added MMRM analysis for all actigraphy endpoints Added 95th percentile of cadence actigraphy endpoint for Screening age strata subgroup analysis
		To correct typographical errors in the subgroup analysis for number of skills endpoints	Section 6.4.1 Removed MMRM description for NSAA total score Added the description of Binomial with logit link function
		To clarify the analysis for AEs of interest	Section 6.7.1 Added summary analysis for AEs of interest using incidence of all-causality adverse event (by severity) and SAEs Updated the interval duration for AE of interest by both cluster terms and the component PTs.
		To update subgroup analysis redefining Baseline NSAA total score groups by using median instead of tertile, and delete the analysis reporting p value for strata by treatment interaction for Baseline NSAA total score strata and Region.	Section 6.5.3, Appendix 1 Changed the definition of Baseline NSAA total score subgroups from tertiles-based to median-based. Removed the analysis to report p value of Baseline NSAA total score by treatment interaction, and Region by treatment interaction

		To clarify the analyses for select laboratory parameter	Section 6.7.2 Updated the summaries for CK, GGT, platelets, and creatinine by using data without normalization Updated shift table category
		To clarify the analyses for vital signs and ECG	Section 6.7.3, 6.7.4, Appendix 2.1 Removed text "(excluding unscheduled and early termination visits)" Clarified the algorithm for handling multiple values observed within a window Updated visit window at Week 2, Day14
		To clarify age calculation for different scenarios	Across the SAP Clarified screening age and age at dosing will be presented as integer for the demographic summary, rounded to one decimal place for baseline characteristic summary and statistical model analysis.
		To align the immune assay name across documents	Sections 3.3.3, 6.3.7, Appendix 1, Appendix 2 Changed ELISpot to T cell response

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study C3391003. This SAP specifically covers the analyses to be performed for the primary analysis that is to occur when all participants have completed visits through Year 1 Week 52 (or withdrawn from the study prior to Year 1 Week 52). There will be 2 additional SAPs to address other planned and optional analyses:

- One SAP will cover the analyses for the Cohort 2 delayed treatment and long-term safety and efficacy analyses.
- One SAP will cover the analyses for the two potential interim analyses (IAs) (See Section 7).

This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

2.1. Study Objectives, Endpoints, and Estimands

Only the study objectives, endpoints and estimands for the Primary Analysis through Week 52 will be presented in this SAP. The objectives for the Cohort 2 delayed treatment and long-

term safety and efficacy parts of the study will be presented in an additional SAP, as noted above.

2.1.1. Efficacy Objectives, Estimands, and Endpoints

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
To demonstrate superior efficacy of treatment with fordadistrogene movaparvovec as compared to placebo based on change from Baseline in the North Star Ambulatory Assessment (NSAA).	Change from Baseline at Week 52 in the NSAA total score.	Population: Boys with a genetic diagnosis of Duchenne muscular dystrophy (DMD) who are ambulatory and age ≥4 to <8 years; Variable: Change from Baseline at Week 52 in the NSAA total score; • Intercurrent event(s) and missing data: The potential intercurrent events are death or loss of ambulation. The intercurrent events and missing data will be handled as described below: • Death or loss of ambulation: NSAA total score will be set to 0 for all scheduled study visits after death or loss of ambulation (if not done after LoA). • Discontinuation from study: missing data from visits after a participant discontinues from the study (with the exception of death) will not be explicitly imputed. • Missing data from a participant not able to perform the NSAA due to acute illness or injury considered to be transient, will be assumed to be missing at random and will not be imputed. Population-level summary: difference in mean changes from Baseline at Week 52 in the NSAA total score between fordadistrogene movaparvovec and placebo.
Secondary:	***Secondary:***	***Secondary:***

Objectives	Endpoints	Estimands
To quantify the mini-dystrophin expression level in the muscle of participants treated with fordadistrogene movaparvovec.	Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using a liquid chromatography mass spectrometry (LCMS) assay.	Population: Boys with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years; Variable: Each secondary endpoint; • Intercurrent event(s) and missing data: The potential intercurrent events are death and loss of ambulation. The intercurrent events and missing data will be handled as described below: • Loss of ambulation or death: secondary endpoints related to NSAA scores for individual skills (i.e.,10 meter run/walk velocity, rise from floor velocity, number of skills gained, and number of skills either improved or maintained) will be set to 0 for all scheduled study visits after loss of ambulation or death (if not done after LoA). • Discontinuation from Study: missing data from visits after a participant discontinues from the study (with the exception of death) will not be explicitly imputed. • Missing data from a participant not being able to perform the NSAA due to acute illness or injury, will not be explicitly imputed. • For all other secondary endpoints (i.e., mini-dystrophin, CK concerntration, PODCI), missing data will not be explicitly imputed regardless of the causes. Population-level summary: difference in means between fordadistrogene movaparvovec and placebo for each secondary endpoint.
To characterize the distribution of mini-dystrophin expression in the muscle of participants treated with fordadistrogene movaparvovec .	Change from Baseline in percent of muscle fibers expressing mini-dystrophin in biceps brachii muscle biopsies at Day 360 (Week 52) as assessed by immunofluorescence.	
To characterize the change in serum creatine kinase (CK) concentration in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in serum CK concentration.	
To characterize the skills gained, based on the individual items of the NSAA, in participants treated with fordadistrogene movaparvovec as compared to placebo.	Number of skills gained at Week 52 based on the individual items of the NSAA.	
To characterize the skills either improved or maintained, based on the individual items of the NSAA, in participants treated with fordadistrogene movaparvovec as compared to placebo.	Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.	
To characterize the 10-meter run/walk velocity in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in the 10 meter run/walk velocity.	
To characterize the rise from floor velocity in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in the rise from floor velocity.	
To characterize the functional health status in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in the Modified Pediatric Outcomes Data Collection Instrument (PODCI): Transfer and Basic Mobility Core Scale (Pediatric Parent).	
	Change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent).	

Objectives	Endpoints	Estimands
Tertiary/Exploratory:	**Tertiary/Exploratory:**	
To assess the systemic immune response (humoral and cellular) to dystrophin in participants treated with fordadistrogene movaparvovec .	Immune response (anti-drug antibodies (ADA) to mini-dystrophin and enzyme-linked immune absorbent spot (ELISpot)) to mini-dystrophin through Year 1 Week 52.	N/A
To assess the systemic immune response (humoral and cellular) to the AAV9 capsid in participants treated with fordadistrogene movaparvovec	Immune response (ADA, ELISpot, and NAb) to AAV9 through Year 1 Week 52.	N/A
To characterize the change in ankle range of motion in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in passive ankle range of motion (dorsiflexion).	N/A
To characterize real-life function in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in real-life function parameters as assessed by actigraphy.	N/A
To tabulate loss of ambulation in participants treated with fordadistrogene movaparvovec compared to placebo.	Loss of ambulation through Week 52.	N/A
To characterize pulmonary function in participants treated with fordadistrogene movaparvovec as compared to placebo.	Change from Baseline at Week 52 in %pFVC.	N/A
To characterize health-related quality of life in participants treated with fordadistrogene movaparvovec as compared to placebo	Response to each of the 5 dimensions of the EQ-5D-Y proxy assessment at Week 52	N/A
	Change from Baseline at Week 52 on the EQ visual analog scale (VAS) proxy assessment.	N/A
To characterize caregiver health-related QoL in caregivers of participants treated with fordadistrogene movaparvovec as compared to placebo.	Response to each of the 5 dimensions of the EQ-5D-5L assessment at Week 52.	N/A
	Change from baseline at Week 52 in the EQ-5D-5L VAS assessment.	N/A
	Change from baseline at Week 52 in the EQ-5D-5L index score.	N/A
To evaluate viral vector shedding following a single administration of fordadistrogene movaparvovec.	Quantification of viral vector shedding kinetics of fordadistrogene movaparvovec in whole blood, saliva and urine.	N/A

2.2. Safety Objectives and Endpoints

Objectives	Endpoints
To characterize the safety of treatment with fordadistrogene movaparvovec as compared to placebo.	Incidence, severity and causal relationship of treatment-emergent AEs (TEAEs) (adverse events [AEs] and serious adverse events [SAEs]) through Week 52. Incidence of abnormal laboratory findings and magnitude of change through Week 52. Abnormal and clinically relevant changes through Week 52 in: • Physical exam; • Neurologic exam;

Objectives	Endpoints
	• Weight; • Vital signs; • ECG; • Echocardiogram; • Cardiac MRI • Child Behavior Check List (CBCL).

2.2.1. Primary Estimand(s)

Primary Estimand: difference in mean change from Baseline at Week 52 in the NSAA total score between fordadistrogene movaparvovec and placebo

- Population: Boys with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years;
- Variable: Change from Baseline at Week 52 in the NSAA total score;
- Intercurrent event(s) and missing data: The potential intercurrent events are death or loss of ambulation. The intercurrent events and missing data will be handled as described below:
  - Death or loss of ambulation: NSAA total score will be set to 0 for all scheduled study visits after death. For participants with LOA, if NSAA test is done post LOA (to confirm a LOA), the NSAA total score from that assessment will be used. A value of 0 will be assumed if NSAA test is NOT DONE post a LOA.
  - Discontinuation from study: missing data from visits after a participant discontinues from the study (with the exception of death) will not be explicitly imputed.
  - Missing data from a participant not able to perform the NSAA due to acute illness or injury considered to be transient, will be assumed to be missing at random and will not be imputed.
- Population-level summary: Difference in mean changes from Baseline at Week 52 in the NSAA total score between fordadistrogene movaparvovec and placebo.

2.2.2. Secondary Estimand(s)

- Population: Boys with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years;
- Variable: Each secondary endpoint;

- Intercurrent event(s) and missing data: The potential intercurrent events are death and loss of ambulation. The intercurrent events and missing data will be handled as described below:

  - Loss of ambulation or death: secondary endpoints related to NSAA scores for individual skills (i.e., 10 meter run/walk velocity, rise from floor velocity, number of skills either improved or maintained, and number of skills gained) will be set to 0 for all scheduled study visits after death. For participants with LOA, if the NSAA test is done post LOA, then the individual items from that assessment would be used in analyzing the secondary endpoints. A value of 0 would be assumed for the 17 NSAA items and the 2 velocity assessments only if the NSAA test is NOT DONE post a LOA.

  - Discontinuation from Study: missing data from visits after a participant discontinues from the study (with the exception of death) will not be explicitly imputed.

  - Missing data from a participant not being able to perform the NSAA due to acute illness or injury, will not be explicitly imputed.

  - For all other secondary endpoints (i.e., mini-dystrophin, CK concerntration, PODCI), missing data will not be explicitly imputed regardless of the causes.

- Population-level summary: difference in means between fordadistrogene movaparvovec and placebo for each secondary endpoint.

2.2.3. Additional Estimand(s)

None.

2.3. Study Design

This is a Phase 3, global, multi-center, randomized, double-blind, placebo-controlled study to assess the safety and efficacy of fordadistrogene movaparvovec gene therapy in approximately 99 ambulatory male participants (in the FAS; see Section 4), ages ≥4 to <8 years, with a genetic diagnosis of DMD who are on a stable daily regimen of glucocorticoids.

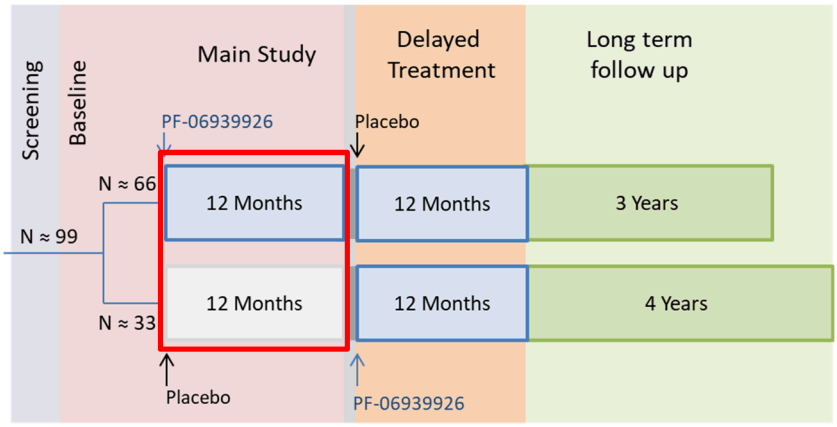
Eligible participants will be randomized into Cohort 1 or Cohort 2 in a 2:1 fashion and stratified by their age at Screening (<6 or ≥6 years old). Study enrollment will be managed to ensure that no more than 55% of dosed participants are in either of the Screening age stratum. Enrollment will be assessed periodically, and if an imbalance is noted, enrollment of the overrepresented stratum may be paused until a more balanced distribution is achieved. In the context of this study, treatment will consist of two single intravenous infusions, one of fordadistrogene movaparvovec and one of placebo, with the timing and sequence as described below:

- Cohort 1 (approximately 66 participants): will receive a single dose of fordadistrogene movaparvovec on Day 1 (Visit 3) and a single dose of placebo at Day

390 (Visit 20). They will be followed for 5 years after the administration of the single dose of fordadistrogene movaparvovec. Total time on study will be approximately 5 years.

- Cohort 2 (approximately 33 participants): will receive a single dose of placebo on Day 1 (Visit 3) and a single dose of fordadistrogene movaparvovec at Day 390 (Visit 20), if they remain eligible. They will be followed for 5 years after the administration of the single dose of fordadistrogene movaparvovec. Total time on study will be approximately 6 years.

Figure 1. Study Schema



2.3.1. Sample Size Determination

The sample size of 99 participants in the FAS (see Section 4) is based on the primary efficacy endpoint of change from Baseline at Week 52 in the NSAA total score. The above sample size (assuming 3 participants will drop out of the study prior to Week 52) will provide 98% power to detect a treatment difference (fordadistrogene movaparvovec minus placebo) of 3.0. These calculations are based on α=0.05 (two-sided), a 3-look group-sequential design with a gamma family (-1) spending function to determine the efficacy boundary, a gamma family (-4) spending function for the non-binding futility boundary, a common standard deviation of 3.5, and using the normal approximation of the test statistic for the comparison between two means.

2.3.2. Treatment Groups and Reporting Periods for Analysis

In the study schematic in **Figure 1**, the study period and treatment groups to be included in the primary analysis are encircled in red.

- Treatment groups:

  1. fordadistrogene movaparvovec – participants randomized to Cohort 1 to receive a single dose of fordadistrogene movaparvovec on Day 1 (Year 1 Day 1).

  2. Placebo – participants randomized to Cohort 2 to receive a single dose of placebo on Day 1 (Year 1 Day 1).

- Reporting Period:

  All analyses will be relative to Day 1 (Year 1 Day 1) investigational product (IP) administration.

  The reporting period will include all data from the day of the Year 1 Day 1 IP administration through Week 52. Specifically, all participant data from Day 1 to the earliest of (1) Day 390 (the upper limit of the Week 52 analysis visit window or (2) one day before the Year 2 Day 1 IP administration.

2.3.3. Siblings

When ≥2 brothers meet all the study entry criteria, they will all be enrolled in the study simultaneously. One of the brothers will be defined as the "participant" and the other(s) will be defined as the "sibling(s)". The sibling(s) will not be randomized but they will receive the same treatment with approximately the same timing (as long as the siblings were strictly separated from each other until both have received IP) and sequence based on the Cohort to which the participant is randomized. The sibling(s) will participate fully in the double blind study as a participant, complete all visits and evaluations, and comply with all protocol requirements. Data from the sibling(s) will not contribute to the main analyses of the primary and secondary endpoints. A supplementary analysis of the primary endpoint, NSAA, will include data from the sibling(s). Data from the sibling(s) will be included in all analyses of safety.

For analysis purposes, the "participant" and the "sibling" will be identified by specific ranges of randomization numbers. Two separate randomization lists will be created; one for participants age <6 years and one for participants age ≥ 6 years. Each eligible participant will be randomized and receive a randomization number from the appropriate randomization list starting with the lowest randomization number. Sibling(s) will be manually assigned a randomization number in the IRT system by the IRT support team. The IRT support team will start at the end of the appropriate randomization list and working backward select the first un-assigned randomization number that will provide the same treatment as that randomly assigned to the participant.

- "Participants" will be those with a randomization number from 1-300 or 1001-1300, depending on their stratum assignment.

- "Siblings" will be those with randomization numbers from 301 to 996 or 1301-1996, depending on their stratum assignment.

If the participant is randomized within the first approximately 15 participants (with the potential to collect a maximum of 33 if needed) collecting muscle biopsies, muscle biopsies will be collected from him and his sibling(s). Biopsy data from the sibling(s) will be excluded from the main analyses of mini-dystrophin in this study, but will be included in supplementary analyses of the secondary endpoints.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint(s)

Change from Baseline at Week 52 in the NSAA total score.

The NSAA is a 17-item test that grades performance of various functional skills using the following scale: 0 (unable to achieve independently), 1 (modified method but achieves goal independent of physical assistance from another), and 2 ("normal"- no obvious modification of activity) [Mazzone et al., 2009][2]. The NSAA total score is calculated as the sum of the individual item responses and ranges from 0 to 34 with higher scores indicating better function.

If one or more of the 17 individual items is missing, the total score is set to missing.

3.2. Secondary Endpoint(s)

1. Change from Baseline in percent normal mini-dystrophin transgene protein expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using an LC-MS assay

   The LC-MS assay measures the LLQVAVEDR (LLQV) peptide that detects full-length endogenous dystrophin as well as the mini-dystrophin transgene protein. The expression level will be provided from the vendor and is expressed as %normal, with normal defined by full length dystrophin from non-dystrophic control samples. Levels below the LLOQ will be imputed as 0.5*LLOQ. The LC-MS assay also measures the LEMPSSLMLEVPTHR (LEMP) peptide which quantifies only the mini-dystrophin transgene levels. The baseline LEMP peptide level in the biceps brachii muscle biopsy is expected to be below the LLOQ due to the absence of the mini-dystrophin transgene prior to treatment.

2. Change from Baseline in percent of muscle fibers expressing mini-dystrophin transgene protein in biceps brachii muscle biopsies at Day 360 (Week 52) as assessed by immunofluorescence.

   Muscle fibers expressing mini-dystrophin transgene protein will be evaluated by immunofluorescent staining using the mini-dystrophin specific antibody that only recognizes the mini-dystrophin transgene protein.

   For the participant in Study C3391003 , a global threshold for calculating the percentage of mini-dystrophin positive fibers was applied based on all baseline samples from the 19 ambulatory participants

3. Change from baseline at Week 52 in serum CK concentration.

   The CK results reported by the central laboratory and each local laboratory will be converted to conventional units of measurement, if necessary. These unit-standardized results will be used for analysis purposes.

4. Number of skills gained at Week 52 based on the individual items of the NSAA.

   The number of skills gained at Week 52 is the total number of skills with a response of 0 at Baseline and a response of either 1 or 2 at Week 52.

5. Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.

   The number of skills either improved or maintained at Week 52 is the total number of skills with:

   - A response of 0 at Baseline and a response of either 1 or 2 at Week 52, or
   - A response of 1 at Baseline and a response of 1 or 2 at Week 52, or
   - A response of 2 at Baseline and a response of 2 at Week 52.

6. Change from Baseline at Week 52 in the 10 meter run/walk velocity.

   Velocity in meter/second is defined as 10 times the reciprocal of the time to complete the 10 meter run/walk test. For participants with a score of 0 on the 10 meter run/walk item (NSAA item 17), velocity will be set to 0. For participants with a missing score on the 10 meter run/walk item (NSAA item 17), velocity will be set to missing.

7. Change from Baseline at Week 52 in the rise from floor velocity.

   Velocity is defined as the reciprocal of the time to rise from floor. For participants with a score of 0 on the rise from floor item (NSAA item 12), velocity will be set to 0. For participants with a missing score on the rise from floor item (NSAA item 12), velocity will be set to missing.

8. Change from Baseline at Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent)

   The Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent) consists of 11 items and assesses a participant's ability to walk, stand, and perform activities of daily living. The scale produces an independent, standardized score ranging from 0-100, with lower scores representing lower levels of function.

   The Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent) standardized score is calculated as described in Appendix 2.2.1

9. Change from baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent).

   The Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent) consists of 21 items and assesses a participant's ability to walk, stand, and perform

activities of daily living. The scale produces an independent, standardized score ranging from 0-100, with lower scores representing lower levels of function.

The Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent) standardized score is calculated as described in Appendix 2.2.1.

3.3. Other Endpoint(s)

Protocol specified tertiary/exploratory endpoints through Week 52 are defined below.

3.3.1. Efficacy Endpoints

1. Change from Baseline at Week 52 in passive ankle range of motion (dorsiflexion).

   The degrees of passive dorsiflexion will be recorded for the left and right ankle.

2. Change from Baseline at Week 52 in real-life function parameters as assessed by actigraphy.

   The following select set of daily measures from the 14 day observation period for each timepoint (Baseline, Weeks 9, 18, 35, and 52) will be analyzed:

   - Steps per day (steps);
   - 95th percentile of cadence (steps/min);
   - Median cadence (steps/min);
   - Percent time in high activity (%).

   For each participant and for each parameter, the mean value across the daily measures will be calculated at each visit. If any day was considered non-compliant, the values from that day will not be included in the calculation of the mean. If a participant has at least 4 compliant days within the monitoring period, then the average across the compliant days will be included in the statistical analysis, otherwise, they will be treated as missing for that monitoring period (visit). These mean values will be used for the analysis of efficacy.

   Compliance for each day is defined as:

   - At least 22 hours of data collected on that day, which corresponds to at least 90% of data capture in a day;
   - At least 300 steps recorded on that day;
   - At least 100 active minutes recorded on that day;
   - At least 30 steps within 5 consecutive hours (9am-7pm) recorded on that day.

3. Loss of ambulation through Week 52.

   Loss of ambulation will be defined as:

   - A caregiver report that the participant is not currently able to walk to perform activities of daily living (as determined by the Lowes Lab Ambulatory Status Algorithm), AND

   - Inability to perform the walk item on the NSAA (unless considered temporary due to acute illness or injury) on the visit following the date on which the caregiver stated the participant lost the ability to ambulate.

   The date for loss of ambulation will be recorded as the date reported by the caregiver as the last date on which the participant was able to walk to perform activities of daily living. This information will be collected on the same days that the NSAA is evaluated.

4. Change from Baseline at Week 52 in %pFVC

   Note: Only collected in participants ≥6 years old at Screening. Spirometry will be performed using standardized equipment in accordance with the American Thoracic Society/European Respiratory Study Task Force: standardization of lung function testing guidelines 2005 [Miller et al., 2012]. Sufficient forced expiratory maneuvers (up to a maximum of 6) will be performed to produce at least 3 technically adequate tracings. The best (largest) FVC measurement from the set of 3 will be used to determine the FVC and the %pFVC according to age, height, race and gender [Quanjer et al., 2012] that are recorded on the CRF.

5. Response to each of the 5 dimensions of the EQ-5D-Y Proxy assessment at Week 52

   The EQ-5D-Y Proxy is a recently developed generic instrument that measures the health status of children. The measure is completed by a caregiver and captures how he or she rates the health of the child. It was adapted from the original EQ-5D questionnaire developed by the EuroQol Group. The EQ-5D-Y Proxy includes five dimensions: mobility (walking around), selfcare (taking care of him/herself), usual activities (doing usual activities), pain/discomfort (having pain or discomfort), and anxiety/depression (feeling worried, sad or unhappy). Responses record three levels of severity: no problems, some problems, a lot of problems.

   There is currently no index score for EQ-5D-Y, but if one becomes available, this will be included as an endpoint.

6. Change from Baseline at Week 52 on the EQ visual analog scale (VAS) proxy assessment.

   The EQ-5D-Y Proxy also includes a standard vertical 20 cm visual analogue scale (EQ VAS) for recording current health-related quality of life on a scale from 0 to 100, with 0 representing the worst and 100 the best health state he or she can imagine.

3.3.2. QoL of Caregivers of Participants

1. Response to each of the 5 dimensions of the EQ-5D-5L assessment at Week 52 (caregivers of participants).

   The EQ-5D-5L will be completed by caregivers regarding their own quality of life. The EQ-5D-5L descriptive system is comprised of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 5 response levels: no problems, slight problems, moderate problems, severe problems, unable to/extreme problems.

2. Change from baseline at Week 52 in the EQ-5D-5L VAS assessment (caregivers of participants).

   The EQ-5D-5L also includes a standard vertical 20 cm VAS for recording current health related quality of life on a scale from 0 to 100, with 0 representing the worst and 100 the best health state imaginable.

3. Change from baseline at Week 52 in the EQ-5D-5L index score (caregivers of participants).

   The EQ-5D-5L index score is a single number summary of the responses to the 5 dimensions and reflects how good or bad a health state is according to the preferences of the general population of a country/region. The index score is derived by applying a formula that attaches values (weights) to each of the levels in each dimension. The EuroQol Group develops and maintains a collection of index values (weights) for all possible EQ-5D health states for specific countries/regions.

3.3.3. Immune Response Endpoints

1. Immune response (anti-drug antibodies [ADA] and T cell response) to mini-dystrophin transgene protein through Year 1 Week 52.

2. Immune response (ADA, T cell response and neutralizing antibodies [NAb]) to AAV9 through Year 1 Week 52.

   ADA and NAb immune responses are provided as Positive or Negative with associated titers. ELISpot immune responses are provided for each of 3 peptide pools as Positive or Negative with associated response levels.

3.3.4. Viral Vector Shedding Endpoints

Whole blood, saliva, and urine samples for viral vector shedding kinetics will be collected in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo). For each randomized participant, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

Viral vector levels (vector genomes /ml), measuring intact and fragmented copies, will be determined in whole blood, saliva and urine using qPCR analysis. Additionally, intact viral vector levels (vector genomes/mL) in saliva and urine samples will be measured as intact copies following treatment with Micrococcal Nuclease (MNase). Viral vector shedding results below the lower limit of quantification (BLQ) for each matrix are considered negative or "undetectable. Section 6.3.8 describes the approach for handling results that are undetectable.

For each of the 5 viral vector level profiles, one without MNase treatment for whole blood, one without MNase for saliva, one with MNase for saliva, one without MNase for urine, and one with MNase for urine, the following endpoints will be determined:

- Peak viral vector levels (vg/ml) post fordadistrogene movaparvovec administration.

  Defined as the largest detectable result collected prior to the first set of 2 consecutive negative results.

- Time in weeks to peak viral vector shedding post fordadistrogene movaparvovec administration.

  Defined as the time in weeks from the date of fordadistrogene movaparvovec administration to the peak viral vector result defined above.

- Time in weeks to undetectable viral vector (time to clearance of viral vector) from date of fordadistrogene movaparvovec administration.

  The first set of 2 consecutive negative results is identified and then time to undetectable viral vector is defined as the time in weeks from the date of fordadistrogene movaparvovec administration to the first of the 2 consecutive negative results identified. If at the time of analysis, the last result is positive or negative results have not been confirmed, the time is recorded at the last date on which a sample for the particular matrix occurs and will be marked as censored for the analysis, meaning the time to undetectable viral vector clearance is at least that value.

- Time in weeks to the last undetectable viral vector from date of fordadistrogene movaparvovec administration

  The first set of 2 consecutive negative results is identified and then time to last undetectable viral vector is defined as the time in weeks from the date of fordadistrogene movaparvovec administration to the last of the 2 consecutive negative results. If at the time of analysis, the last result is positive or negative results have not been confirmed, the time is recorded at the last date on which a sample for the particular matrix occurs and will be marked as censored for the analysis, meaning the time to undetectable viral vector clearance is at least that value.

3.4. Baseline Variables

3.4.1. Covariates and Stratification Variables

- Baseline for the primary endpoint: Baseline NSAA total score is defined as the last non-missing NSAA total score collected prior to Year 1 IP administration.

- Baseline for secondary and exploratory endpoints: Baseline is defined as the last non-missing assessment collected prior to Year 1 IP administration.

- Screening age (years) covariate: The screening age covariate is defined as the participant's age (as calculated based on month and year of birth) on the day of the Screening visit. Screening age will be calculated to one decimal (eg, 7 years and 4 months will be 7.3 years).

- The participant's Screening age rather than Screening age stratum will be used in all efficacy analyses, unless specified otherwise.

3.4.2. Other Baseline Variables to be Summarized

1. Demographic characteristics including age, gender, race, and ethnicity, where age is calculated as age in years at the Screening visit.

2. Age (years) at dosing with IP on Year 1 Day 1, where age is calculated and rounded to one decimal.

3. Screening age strata (<6 or ≥ 6 years old): Screening age strata will be based on the randomization group entered in CRF by a site that identifies the age strata for a participant based on age at screening.

4. Physical measurements at Baseline include height (cm) and weight (kg) where Baseline is defined as the last non-missing assessment collected prior to Day 1 (Year 1 Day 1).

5. Other participant characteristics including:

    - Details of DMD genetic results.

    - Background glucocorticoid regimen (including specific medication and daily dose in mg/kg, and duration of current glucocorticoid regimen use) at the Screening visit, and age at initiation of any glucocorticoid use (years/months).

    - Duration of glucocorticoid use (months) for the glucocorticoid regimen the participant was receiving at Screening.

    - Age at initiation of any glucocorticoid use.

    - Enrollment geographical region (eg, North America, Western Europe, Eastern Europe, and Asia) and country within each region.

6. General medical history, including diseases or syndromes that are stopped before Screening ("before") or ongoing ("ongoing"). The Medical Dictionary for Regulatory Activities (MedDRA) will be used to code the disease/syndrome.

7. Medications taken prior to the first dose.

3.5. Safety Endpoints

For safety endpoints, unless otherwise specified, Baseline is defined as the last non-missing assessment collected prior to Day 1 (Year 1 Day 1) IP administration. For vital signs, baseline is defined as the assessment collected prior to dosing (0 minutes) on Day 1.

3.5.1. Adverse Events

All nonserious AEs and SAEs occurring in a participant during the active collection period, which begins after obtaining informed consent as described in Section 8.3.1.2 of the protocol, will be recorded on the AE section of the CRF. MedDRA will be used to classify all AEs with respect to system organ class (SOC) and preferred term (PT).

An AE is considered a treatment-emergent adverse event (TEAE) if the event started during the reporting period for the Primary Analysis through Week 52 (Section 2.3.2).

3.5.2. Laboratory Data

The following safety laboratory tests will be collected. Analyses for banked biospecimens are not in scope for this SAP.

Table 2. Protocol Required Safety Laboratory Assessments

CENTRAL LABORATORY TESTING		
Clinical Safety		
Hematology	**Urinalysis**	**Other**
Hemoglobin Hematocrit Red blood cell (RBC) count and morphology Platelet count White blood cell count (and morphology as applicable) Total neutrophils (Abs) Absolute neutrophils Eosinophils (Abs) Monocytes (Abs) Basophils (Abs) Lymphocytes (Abs) Red blood cell indices (mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration)	PH Glucose (qual) Protein (qual) Blood (qual) Ketones Nitrites Leukocyte esterase Microscopy and culture[0]	Prothrombin time (PT) activated partial thromboplastin time C-reactive protein Lipase Amylase Cystatin C Haptoglobin[b]
Chemistry and Hepatic Safety		
BUN and Creatinine Glucose Calcium Sodium Potassium Chloride Total CO2 (Bicarbonate) AST, ALT Total Bilirubin (direct and indirect bilirubin) Alkaline phosphatase Uric Acid Albumin Total protein Serum Phosphorus Gamma glutamyl transferase (GGT) Glutamate dehydrogenase (GLDH)		
For Screening (Visit 1) and Day 360 (Visit 19) Only		
International normalized ratio (INR) Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen Hepatitis C antibody		
For Post IP Intensified Safety Monitoring (at Year 1 and Year 2)		
Complement biomarkers eg, C3 and C4, additional exploratory[c] Haptoglobin – analyzed by local laboratory on Days 2 and 4 (Visits 4 and 5) in Year 1 and on Days 391 and 393 (Visits 21 and 22) in Year 2 for sites in Japan. Urine biomarkers		

Table 2. Protocol Required Safety Laboratory Assessments

Other Assessments	
Immunogenicity: NAb to AAV9; ELISpot to AAV9; ADA to AAV9; ELISpot to mini-dystrophin; ADA to mini-dystrophin	
Viral vector shedding (whole blood, saliva, and urine)	
Cardiac troponin I	
Creatine kinase	
Conditional Testing	
Genetic screening for aHUS-Central Laboratory, if needed as per Section 6.5.1 in the Protocol	
Local assessment of NT-ProBNP/BNP, if needed as per Section 8.2.7 in the Protocol	
LOCAL AND CENTRAL LABORATORY TESTING	
Local Laboratory	
Hematology: as per clinical safety panel, including blood smear for morphology. Absolute neutrophils are not required	Day 6 to 10 (Visits 6 to 10) in Year 1 Day 395 to 399 (Visits 23 to 27) in Year 2
Chemistry and hepatic safety: at a minimum, creatinine, BUN(or blood urea if BUN cannot be performed), calcium, sodium, potassium, chloride, total CO2 (bicarbonate), uric acid and serum phosphorus; but excluding AST and ALT- sensitive clinical data	Day 6 to 10 (Visits 6 to 10) in Year 1 Day 395 to 399 (Visits 23 to 27) in Year 2
Cystatin C (when possible)	Day 6 to 10 (Visits 6 to 10) in Year 1 Day 395 to 399 (Visits 23 to 27) in Year 2
Urinalysis: as per clinical safety panel	Day 6 to 10 (Visits 6 to 10) in Year 1 Day 395 to 399 (Visits 23 to 27) in Year 2
Cardiac troponin I, (or cardiac troponin T if cardiac troponin I is not available)	Baseline Visit (Visit 2), Day 2 (Visit 4), Day 4 (Visit 5), Day 6 (Visit 6), Day 8 (Visit 8), and Day 10 (Visit 10) in Year 1 Day 390 (Visit 20), Day 391 (Visit 21), Day 393 (Visit 22), Day 395 (Visit 23), Day 397 (Visit 25), and Day 399 (Visit 27) in Year 2
Serum creatinine	Baseline Visit, Day 2 and Day 4 (Visits 2, 4 and 5) in Year 1 Day 390 to Day 393 (Visits 20 to 22) in Year 1
Local Laboratory for Japan Only	
Local labs as described above	Day 2 to Day 10 (Visit 4 to Visit 10) in Year 1 Day 391 to Day 399 (Visits 21 to 27) in Year 2
Haptoglobin	Day 2 and Day 4 (Visit 4 and Visit 5) in Year 1 Day 391 and Day 393 (Visits 21 and 22) in Year 2
Local Laboratory for Russia Only	
Chemistry and hepatic safety	Baseline (Visit 2), Day 2 to Day 240 (Visit 4 to Visit 17) in Year 1[d,e] Day 390 to Day 629 (Visit 20 to Visit 34) in Year 2[d,e]
Hematology	Screening Visit (Visit 1), Day 2 to Day 21 (Visit 4 to Visit 12), Day 34 (Visit 13), Day 60 (Visit 14), Day 90 to Day 240 (Visit 15 to Visit 17) and Day 360 (Visit 19) in Year 1[f] Day 391 to Day 410 (Visit 21 to Visit 29), Day 423 (Visit 30), Day 449 (Visit 31) and Day 479 to Day 629 (Visit 32 to Visit 34) in Year 2

Table 2. Protocol Required Safety Laboratory Assessments

Cystatin C (when possible)	Day 2 to Day 240 (Visit 4 to Visit 17) in Year 1 Day 390 to Day 629 (Visit 20 to Visit 34) in Year 2
GLDH (when possible)	Day 2 to Day 240 (Visit 4 to Visit 17) in Year 1 Day 390 to Day 629 (Visit 20 to Visit 34) in Year 2
Urinalysis	Day 1 to Day 21 (Visit 3 to Visit 12) in Year 1 Day 390 to Day 410 (Visit 20 to Visit 29) in Year 2
Cardiac I, (or cardiac troponin T if cardiac troponin I is not available)	Baseline Visit (Visit 2), Day 2 (Visit 4), Day 4 (Visit 5), Day 6 (Visit 6), Day 8 (Visit 8), and Day 10 (Visit 10), Day 21 to Day 120 (Visit 12 to Visit 16) in Year 1. Day 390 to Day 509 (Visit 20 to Visit 33) in Year 2
Coagulation	Screening Visit (Visit 1), Day 2 to Day 21 (Visit 4 to Visit 12), Day 34 (Visit 13), Day 60 (Visit 14), Day 90 to Day 240 (Visit 15 to Visit 17) in Year 1 Day 391 to Day 410 (Visit 21 to Visit 29), Day 423 (Visit 30), Day 449 (Visit 31) and Day 479 to Day 629 (Visit 32 to Visit 34) in Year 2
Central Laboratory	
Clinical safety (not for Japan)	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 392 (Visits 21 and 22) in Year 2
Chemistry and hepatic safety (not for Japan)	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 392 (Visits 21 and 22) in Year 2
Urinalysis (not for Japan)	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 392 (Visits 21 and 22) in Year 2
GLDH	Day 9 (Visit 9) at Year 1 Day 398 (Visit 26) at Year 2
C3, C4	Days 6 to 10 (Visits 6 to 10) at Year 1 Day 395 to 399 (Visits 23 to 27) in Year 2
Cardiac troponin I	Day 7 (Visit 7) at Year 1 Day 396 (Visit 24) at Year 2

a. Only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase. Culture to be done locally.
b. Only for the Screening Visit (Visit 1) and for Day 360 Visit (Visit 19).
c. Additional biomarkers, such as ferritin, will be included so long as blood volume limits are not exceeded.
d. Only creatinine is required at Baseline Visit (Visit 2) in Year 1 and on Day 390 (Visit 390) in Year 2.
e. ALT and AST will not be analyzed locally, those samples will be sent to the central laboratory to prevent the results being shared with the site or the Sponsor (Section 6.3.).
f. On Day 360 (Visit 19) the results of neutrophils and platelets are considered sensitive clinical data and are not shared with the site or the Sponsor. They will only be shared with the unblinded medical monitor so they can perform the determination of eligibility for Year 2 IP administration (Section 6.3.3). The local laboratories at the Russian sites will follow the same process.

The results reported by the central laboratory and each local laboratory will be converted to conventional units of measurement, if necessary. If there is a local and central laboratory

collection on the same day, the central laboratory value will be used for analysis. These unit-standardized results will be used for analysis purposes.

The following select laboratory parameters will have additional analyses (Section 6.7.2): GLDH, CK, C3, C4, creatinine, platelets, and cardiac Troponin I (cTn-I)

3.5.3. Other Safety Endpoints

1. Complete physical examination and brief physical examination

   If any finding on the physical examination is considered by the investigator to be 'clinically significant', the event is to be recorded as an AE, as appropriate.

2. Complete neurological examination and brief neurological examination

   If any finding on the neurological examination is considered by the investigator to be 'clinically significant', the event is to be recorded as an AE, as appropriate.

3. Vital Signs

   Vital sign parameters include body weight, height, body temperature, pulse rate, respiratory rate, O2 saturation (during 7-day hospitalization post IP administration), and supine blood pressure (systolic and diastolic).

4. Electrocardiogram (ECG)

   A single 12-Lead ECG produces the following parameters, as assessed by a central reader: heart rate, PR, QT, corrected QT intervals (ie, QTcF corrected using Fridericia's formula), and QRS complex.

5. Echocardiogram

   The parameters from the echocardiogram include:

   - LV Fractional Shortening: (%)
   - LVEF: %
   - Myocardial longitudinal strain -Global: %
   - Myocardial circumferential strain – Global: %
   - LV mass (g)
   - LV end diastolic and end systolic volume (mL)
   - Wall motion abnormalities (normal/ Hypokinetic/ Hyperkinetic/ Dyskinetic/ Akinetic/ Indeterminate)

- Location: LV Basal Anteroseptal, LV Mid Anteroseptal, LV Basal Inferolateral, LV Mid Inferolateral, LV Basal Inferoseptal, LV Mid Inferoseptal, LV Apical Septal, LV Basal Anterolateral, LV Mid Anterolateral, LV Apical Lateral, LV Basal Inferior, LV Mid Inferior, LV Apical Inferior, LV Basal Anterior, LV Mid Anterior, LV Apical Anterior.

- Wall thickness (mm)
  - Location: Interventricular Septum, LV Basal Inferolateral
- Pericardial effusion (present/absent)
  - Location: Pericardial Effusion Indicator: Present, Absent, Not Evaluable
- Pericardial effusion, thickness (mm)

6. Cardiac MRI

   The parameters from the cardiac MRI include:

   - LVEF (%)
   - Myocardial strain parameters include:
     - Global longitudinal strain (%)
     - Global circumferential strain (%)
     - Global radial strain (%)

     Myocardial strain measures the degree of myocardial deformation from relaxed to contractile state and is expressed as a percentage. Following the different directions in which the myocardium deforms, longitudinal, circumferential and radial strain can be calculated. Longitudinal strain represents the longitudinal shortening from the base to the apex, and it is expressed by negative values. Circumferential strain represents the shortening along the circular perimeter, and it is consequently represented by negative values. Radial strain is the thickening myocardial deformation towards the center of the left ventricular cavity, and it is expressed by positive values.

   - Myocardial fibrosis as assessed by number of LGE positive segments

     Participants who have a contraindication to the use of gadolinium will be allowed to have an MRI without contrast. In this case, number of LGE positive segments will be missing.

7. Child Behavior Check List (CBCL)

The Child Behavior Check List (CBCL) is a questionnaire designed to assess behavior problems and social competency in children. There are two versions: the 100-item pre-school questionnaire for ages 1.5 to 5 years, and the 120-item school-age questionnaire for ages 6 to 18 years. For this study, scores on the Withdrawn (pre-school) or Withdrawn/Depressed (school-age) syndrome scale and on the Internalizing global scale (both versions) will be examined as high-risk behaviors or dysfunction. Higher scores on the CBCL indicate higher levels of problematic behaviors or dysfunction. The CBCL scoring algorithm allows for a participant's scores to be standardized using scores from a normal population. These standardized scores are referred to as T-scores. A threshold of ≥65 on the T-scores for the Withdrawn and Withdrawn/Depressed syndrome scales and a threshold of ≥60 on the and Internalizing global scale indicate clinically significant behaviors.

The specific binary endpoints to be assessed are:

- Withdrawn T-score or Withdrawn/Depressed Syndrome T-Score ≥65;
- Internalizing Global Scale T-Score ≥60.

8. Investigational Product Administered

The three endpoints below will be used to describe the amount of IP administered.

- The actual total administered dose of fordadistrogene movaparvovec in vg will be calculated as

$$\text{Actual total administered dose (vg)} = \text{planned dose (vg)} * \frac{\text{administered volume (ml)}}{\text{planned volume (ml)}}$$

- The actual administered dose of fordadistrogene movaparvovec in vg/kg will be calculated as

$$\text{Actual administered dose (vg/kg)} = \frac{\text{actual total administered dose (vg)}}{\text{weight at Baseline (kg)}}$$

- The percent of planned dose administered will be calculated as

$$\text{Percent planned dose administered (\%)} = 100\% \frac{\text{actual total administered dose (vg)}}{\text{planned dose (vg)}}$$

Note that the administered volume will be less than the planned volume if the infusion is stopped prematurely.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

For purposes of analysis, the following populations are defined:

Population	Description
Enrolled	All participants who sign the Informed Consent Document.
All Randomized	All participants, including siblings and those meeting exclusion criterion 15, who were randomly assigned to Cohort 1 (initially fordadistrogene movaparvovec) or Cohort 2 (initially placebo).
Full Analysis Set (FAS)(through Week 52)[a]	All participants, excluding siblings and those meeting exclusion criterion 15, who were randomly assigned and received a single dose of IP on Day 1 (Year 1 Day 1). Participants will be analyzed according to the cohort to which they were randomized.
Safety Analysis Set (through Week 52)	All participants, including siblings and those meeting exclusion criterion 15, who were randomly assigned and received a single dose of IP on Day 1 (Year 1 Day 1). Participants will be analyzed according to the IP they actually received. Note: Per protocol amendment #6 and protocol amendment 12 (Section 5.2 and 10.12), participants in Cohort 2 who had already received IP (ie, placebo) at the time of implementation of the temporary enrolment and dosing pause, and who are retrospectively determined to meet exclusion criterion 15 upon approval of protocol amendment 6 will not be eligible for Year 2 IP (ie, fordadistrogene movaparvovec) administration and will be withdrawn from the study immediately upon determination of non-eligibility. These participants will be included in the Safety Analysis Set (through Week 52); however, they will contribute partial data.

[a] Of note, per the PCD definition in protocol amendment 15, the primary analysis will occur after at least 90 FAS participants complete Day 360 (Visit 19) or discontinue from the study prior to Week 52 if they had received Year 1 IP at least one year prior to the data cutoff.

In addition, as a subset of participants had biopsy samples taken to assess mini-dystrophin levels, and a subset of participants had whole blood, urine and saliva samples taken to assess viral vector shedding kinetics, the following population is defined:

Population	Description
Viral Vector Shedding	For each matrix, all participants, including siblings and those meeting exclusion criterion 15, who were randomly assigned, received a single dose of fordadistrogene movaparvovec on Day 1 (Year 1 Day 1), and who had at least two post-Baseline measurements within the first 7 days after fordadistrogene movaparvovec administration.

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database and classifications will be documented per standard operating procedures.

5. GENERAL METHODOLOGY AND CONVENTIONS

The primary analysis will occur after at least 90 FAS participants complete Day 360 (Visit 19) or discontinued from the study prior to Week 52 if they had received Year 1 IP at least

one year prior to the data cutoff. There are 2 options for IAs, both of which are designed to provide data to support an earlier regulatory submission for BLA/MAA as described in Section 7.
As a general rule, all efficacy analyses including the primary endpoint, secondary endpoints, and other endpoints will be conducted based on all FAS participants regardless of adherence to background or protocol mandated glucocorticoid regimens during the first 52 weeks after study drug infusion, unless specified otherwise.

5.1. Hypotheses and Decision Rules

For the primary endpoint, the null hypothesis is that there is no difference between fordadistrogene movaparvovec and placebo with respect to mean change from Baseline at Week 52 in the NSAA total score. The alternative hypothesis is that fordadistrogene movaparvovec is different from placebo with respect to mean change from Baseline at Week 52 in the NSAA total score.

The experiment-wise Type I error rate of α=0.05 (two-sided) will be controlled using gatekeeping and fixed-sequence procedures for the primary and select secondary endpoints listed below. The hypotheses for the secondary endpoints are similar to those for the primary endpoint.

- Change from Baseline at Week 52 in the 10 meter run/walk velocity.
- Change from Baseline at Week 52 in the rise from floor velocity.
- Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.
- Number of skills gained at Week 52 based on the individual items of the NSAA.

If the null hypothesis for the primary endpoint is rejected, statistical testing proceeds to the hypotheses for the secondary endpoints; otherwise, formal statistical testing in the sense of controlling the experiment-wise Type 1 error rate stops and nominal p-values for secondary endpoints will be reported and interpreted accordingly.

The secondary endpoints will be tested in the order specified above. To maintain the study-wise type 1 error rate, the p value boundary for these secondary endpoint analyses will be the same as the primary analysis as detailed in IA SAP. If the null hypothesis for the first endpoint in the sequence is rejected, statistical testing moves to the next endpoint in the sequence. Statistical testing proceeds to subsequent endpoints in the sequence only if the null hypothesis for the previous endpoint is rejected. If a null hypothesis in the sequence is not rejected, formal statistical testing in the sense of controlling the experiment-wise Type I error rate is stopped for all endpoints later in the sequence and nominal p-values will be reported and interpreted accordingly.

The null hypothesis for the primary and secondary endpoints will be tested at Week 52 using the parameter and variance estimates from the mixed model repeated measures (MMRM) model or the generalized mixed model described in Section 5.2.

If either IA is performed, a group sequential approach will be applied to the efficacy analyses to control Type I error rate across the interim analysis/analyses and the primary analysis. Specifically, a gamma family alpha-spending function with gamma parameter -1 will be used. Additionally, an assessment of futility (non-blinding) based on the primary endpoint will be made at each interim analysis, if performed, using a gamma family spending function with gamma parameter -4.

All other statistical tests for secondary endpoints will be performed and the p value boundary for these secondary endpoint analyses will be the same as the primary analysis as detailed in IA SAP. The hypotheses and additional details on decision rules for the two possible IAs will be provided in a separate IA SAP.

5.2. General Methods

A general description of how the study will be summarized including definitions of treatment groups and reporting period is provided in Section 2.3.2.

5.2.1. Analyses for Continuous Endpoints

5.2.1.1. Mixed Model Repeated Measures (MMRM)

The MMRM model assumes that all random effects in the model are normally distributed. The dependent variable will be the specific endpoint and the model will include fixed effects terms for:

- Treatment group (as a categorical variable);
- Scheduled visit time point (as an ordered categorical variable);
- Interaction between treatment group and scheduled visit time point.

Additional fixed effects (eg, covariates and interaction effects) to be included in the model for specific analyses are given in Section 6. Participant will be the random effect in the model. The restricted maximum likelihood (REML) estimation method will be used with an unstructured covariance matrix to describe the correlation among different visits from the same participant. If there are convergence issues with the model, the following structures will be considered in the order listed below until convergence is obtained:

1. Spatial Power (SP);
2. Autoregressive-1 (AR(1));
3. Compound Symmetry (CS).

The Kenward-Roger degrees of freedom will be used.

The model-adjusted estimates for the endpoint for each treatment group at each specified time point will be provided using the least squares (LS) means calculated based on the average continuous covariate values, standard error of each LS mean, and their 95%

confidence intervals (CIs). The difference in LS means (fordadistrogene movaparvovec minus placebo) will be provided at each specified time point along with corresponding standard error, two-sided p-values (unadjusted for multiplicity), and 95% CIs (unadjusted for multiplicity). .

5.2.1.2. MMRM with Log Transformation

The MMRM approach with a log transformation will be used for endpoints that are markedly skewed and positive. The natural log of the data at each visit will be used to calculate change from Baseline in the log transformed data, (log[post-baseline value] – log[baseline value]) which will be used as the dependent variable in the model. The LS means for each treatment group and the corresponding 95% CIs will be back-transformed (ie, exponentiated) resulting in percent of baseline (ie, percent of baseline = [exp (LS mean)]*100%) values less than 100% representing a decrease from baseline and values greater than 100% representing an increase from baseline

The differences in LS means and 95% CIs will be back-transformed (ie, exponentiated) resulting in a ratio of mean percentages of baseline where a ratio >1 indicates that fordadistrogene movaparvovec has a larger increase relative to placebo.

5.2.1.3. Analysis of Covariance (ANCOVA)

The analysis of covariance (ANCOVA) model assumes that the error term has a normal distribution. The dependent variable will be the specific endpoint and the model will include a term for treatment group (as a categorical variable). Additional terms (eg, covariates and interaction effects) to be included in the model are specified in Section 6.

The model-adjusted estimates for the endpoint for each treatment group will be provided using the LS means, standard error of each LS mean, and their 95% CIs calculated based on the average continuous covariate values. The differences in LS means (fordadistrogene movaparvovec minus placebo) will be provided along with the corresponding standard error, two-sided p-value (unadjusted for multiplicity) and 95% CI (unadjusted for multiplicity).

5.2.2. Analyses for Time-to-Event Endpoints

Time-to-event endpoints will be summarized using the Kaplan-Meier (K-M) method and estimated K-M curves will be displayed graphically. Graphs will describe the number of participants at risk over time. Censoring definitions are provided in Section 3.3.4 under the specific time to event endpoints.

5.2.3. Analyses for Proportions based on Number of Successes

Endpoints defined as the number of successes out of a possible number of tests for each participant at each timepoint will be analyzed using a generalized mixed model assuming a Binomial distribution with a logit link. For example, for the number of skills gained in the NSAA, the endpoint is the number of skills gained out of the number of skills that can be gained (score 0 at Baseline). The maximum likelihood estimation method with Newton Raphson iteration will be used. The fixed effect of treatment group (as a categorical variable) will be included in the model along with any covariates given in Section 6. The effect of

treatment will be examined using the Wald chi-square statistic (CHISQ option). LS means and 95% CIs and the difference in LS means and 95% CIs will be estimated using the z-statistic, by defining degrees of freedom to be infinite in the model (DDFM=NONE). The inverse link transform (ILINK) will be applied to obtain the LS means on the original scale, which will represent average proportions of success.

The estimate of difference in LS means when back-transformed will represent a odds ratio comparing the odds of a success occurring between two treatment groups. In order to represent these proportions as meaningful counts of success, the proportions will be multiplied by the average of the baseline values of the number of tests across all participants, irrespective of treatment group. For example, for number of skills gained, the average baseline number of skills that can be gained will be calculated. Then the back-transformed LS means representing the proportion of successes for each treatment group will be multiplied by this average baseline value, to give a representation of the average number of skills gained for each treatment group, for the population in this study.

5.2.4. Global Statistical Test for Multiple Endpoints

To evaluate the treatment effect more comprehensively, a global statistical test (GST) will be conducted. The information from multiple functional endpoints will be aggregated in a single combined global test by aggregating test statistics from multiple endpoints into a single global test statistic. Because the units of the endpoints are different, the estimated group differences from MMRM will be standardized using a z score.

A permutation test will be performed to assess the chance of observing the mean z score assuming there is no treatment effect. The participants will be shuffled randomly between 2 treatment groups, and the mean observed z score will be calculated for each iteration. This process will be repeated 10,000 times. The standardized z score for each endpoint, mean observed z score across multiple endpoints, and p-value for the GST will be provided.

5.3. Methods to Manage Missing Data

For the MMRM analysis, all available windowed data through Week 52 will be included in the analysis with no explicit imputation of missing data. For participants with the endpoint observed at the primary timepoint, values of the endpoint at other timepoints do not influence the estimate at the primary endpoint and will reduce the variability. For participants with the endpoint missing at the primary timepoint, values at other timepoints influence the estimate at the primary timepoint implicitly. The MMRM analysis is unbiased under the assumption that all missing data are missing at random (MAR) and is valid under the assumption that participants who discontinue would behave similarly to other participants in the same treatment group had they not discontinued. Under Primary Estimand, this assumption is scientifically plausible since fordadistrogene movaparvovec is intended to be used as a gene replacement therapy (ie, disease-modifying). Participants receive a single infusion of investigational product (fordadistrogene movaparvovec or placebo) on Day 1 and thus, discontinuation from treatment is not possible, and it is reasonable to assume that participants who discontinue from the study would behave similarly to other participants in the same treatment group had they not discontinued from the study.

To assess the sensitivity of the MMRM analysis under Primary Estimand to model assumptions and to verify the robustness of the estimates to departures from the assumptions, a copy increments in reference imputation approach will be used [Cro et al, 2016][3]. Missing data in the reference (placebo) group will be imputed under the MAR assumption, while missing data in the fordadistrogene movaparvovec group will be imputed under a missing not at random (MNAR) assumption where the missing data starts from the last non-missing value and then changes to following the differences in the placebo group profile. This assumes that the participant profile in the fordadistrogene movaparvovec groups tracks that of the placebo group, but starting from the benefit already obtained, which reflects the fordadistrogene movaparvovec having a benefit but participants who drop out are then experiencing a disease progression as a worst case scenario.

A tipping point analysis will also be performed to assess the sensitivity of the MMRM analysis under Primary Estimand and assess the impact of missing data.

No imputation for missing data will be performed for other analysis approaches.

5.4. Meaningful Within-Patient Change Threshold

To aid in the interpretation of the treatment effect on the NSAA total score, the Modified Pediatric Outcomes Data Collection Instrument (PODCI): Transfer and Basic Mobility Core Scale (Pediatric Parent), and the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent), the meaningful within-patient change thresholds (MWPC) will be estimated for above outcomes using anchor-based methods as described in a supplemental SAP.

To assess whether the treatment effect for each endpoint occurs in the range that patients' consider to be clinically meaningful, eCDFs of within-patient changes from baseline will be provided for:

- Change from Baseline at Week 52 in the NSAA total score
- Change from Baseline at Week 52 in the Modified Pediatric Outcomes Data Collection Instrument (PODCI): Transfer and Basic Mobility Core Scale (Pediatric Parent)
- Change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent)

For each endpoint separately, the following figure will be generated, the eCDF curves will display endpoint values (both positive and negative) on the horizontal axis, the cumulative proportion of participants experiencing up to that level of change in the endpoint on the vertical axis (separate curves for dadistrogene movaparvovec and placebo). The graphs will be annotated with a range of *MWPC* values and the proportion of patients in each trial arm whose change-from-baseline exceeds one or more values of *MWPC*.

6. ANALYSES AND SUMMARIES

For analysis purposes, all dated assessments will be categorized into analysis windows. Analysis windows for primary, secondary, and other efficacy endpoints are provided in Appendix 2.1.

6.1. Primary Endpoint

6.1.1. NSAA Total Score

Endpoint: Change from Baseline at Week 52 in the NSAA total score

6.1.1.1. Main Analysis

- Estimand strategy: Primary Estimand (Section 2.2.1).
- Analysis set: FAS (Section 4).
- Analysis methodology: Change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 where NSAA is assessed (ie, Weeks 9, 18, 35, 52) with additional fixed effects for Baseline NSAA total score (continuous variable), Screening age (continuous variable), Baseline NSAA total score by visit interaction, and Screening age covariate by visit interaction.

  To test the primary hypothesis, estimates from the MMRM analysis at Week 52 of the mean changes from Baseline, standard error of each LS mean, and 95% confidence intervals along with the mean treatment group difference, two-sided p-value, and two-sided 95% confidence interval for the mean difference will be provided.
- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events (loss of ambulation or death) and missing data from study discontinuation will be handled in the Primary Estimand as described in Section 2.2.1.
- The number of participants (N), mean, standard deviation (SD), median, first quartile (Q1), third quartile (Q3), minimum, and maximum at Baseline and all visits through Week 52 where NSAA is assessed for observed and changes from baseline NSAA total scores will be provided for fordadistrogene movaparvovec and placebo.
- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from Baseline in NSAA total score for Week 52 and all visits through Week 52 where NSAA is assessed.

Graphical displays:

- The fordadistrogene movaparvovec and placebo LS means, and 95% CIs for the LS means at each visit will be displayed graphically.

6.1.1.2. Sensitivity Analysis #1

To assess the impact of missing data on the main analysis under the Primary Estimand (Section 6.1.1.1), missing values will be imputed in this analysis.

- Estimand strategy: Primary Estimand (Section 2.2.1).
- Analysis set: FAS (Section 4).
- Analysis methodology: Change from baseline will be analyzed using a copy increments in reference approach (Section 5.3) including covariates for Baseline NSAA total score (continuous variable) and Screening age covariate (continuous variable).
- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events will be handled as described in Section 2.2.1. Missing data will be imputed using the copy increments in reference approach (Section 5.3).
- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from Baseline in NSAA total score at Week 52.

6.1.1.3. Sensitivity Analysis #2

A tipping point analysis will be performed to assess the impact of missing data on the main analysis under Primary Estimand (Section 6.1.1.1).

6.1.1.4. Sensitivity Analysis #3

There was a quality event investigation (PR2222549) involving Clinical Site 1024 based on quality issues in the assessment of NSAA. Specifically, there were significant quality concerns around NSAA assessments done by one of the raters at this site. To evaluate the impact of these findings on the primary analysis, a sensitivity analysis will be done by excluding all NSAA assessments conducted by this rater.

6.1.1.5. Sensitivity Analysis #4

The difference between screening age and age at dosing due to pause(s) in dosing during the conduct of the study could impact the evaluation of age effect in the model. To assess this impact, a sensitivity analysis of the primary analysis would be conducted by replacing age at screening with age at dosing as the age-based covariate.

6.1.1.6. Supplementary Analysis

This analysis is the same as the main analysis in Section 6.1.1.1 except data from sibling(s) will be added to the data from the FAS if applicable. No graphics will be produced for this analysis.

- Estimand strategy: Primary Estimand (Section 2.2.1).

- Analysis set: FAS (Section 4) plus data from sibling(s) (Section 2.3.3).

- Analysis methodology: Change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 where NSAA is assessed (ie, Weeks 9, 18, 35, 52) with additional fixed effects for Baseline NSAA total score (continuous variable), Screening age covariate (continuous variable), Baseline NSAA total score by visit interaction, and Screening age covariate by visit interaction.

- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.1.

- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and all visits through Week 52 where NSAA is assessed for observed NSAA total scores and changes from baseline will be provided for fordadistrogene movaparvovec and placebo.

- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from Baseline in NSAA total score for all visits through Week 52 where NSAA is assessed.

6.1.1.7. Meaningful Within-Patient Change Threshold

eCDF curves of change from Baseline in the NSAA total score at Week 52 will be provided as described in Section 5.4.

6.2. Secondary Endpoints

6.2.1. Biceps Muscle Biopsies

Endpoints:

- Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using an LC-MS assay (primary peptide is LLQV).

- Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using an LC-MS assay (supplementary peptide is LEMP).

- Change from Baseline in percent of muscle fibers expressing mini-dystrophin in biceps brachii muscle biopsies at Day 360 (Week 52) as assessed by immunofluorescence.

6.2.1.1. Main Analysis

- Estimand strategy: Secondary Estimand (Section 2.2.2).

- Analysis set: FAS (Section 4).
- Analysis methodology: Change from baseline will be analyzed using an ANCOVA model (Section 5.2.1.3) including terms for treatment group, and Screening age covariate (continuous variable).
- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.2
- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline (only for LC-MS assay) and Day 360 (Week 52) for the observed value and change from baseline will be provided for fordadistrogene movaparvovecand placebo.
- The fordadistrogene movaparvovec and placebo LS means, standard error for each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI at Day 360 (Week 52) will be provided.

Graphical displays:

- The distribution of changes from baseline at Day 360 (Week 52) for fordadistrogene movaparvovec and placebo will be displayed graphically using box plots.

6.2.1.2. Supplementary Analysis

This analysis is the same as the main analysis in Section 6.2.1.1 except data from sibling(s) will be added to the data from the FAS if applicable. No graphics will be produced for this analysis.

Endpoints:

- Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using an LC-MS assay (primary peptide is LLQV).
- Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 (Week 52) using an LC-MS assay (supplementary peptide is LEMP).
- Change from Baseline in percent of muscle fibers expressing mini-dystrophin in biceps brachii muscle biopsies at Day 360 (Week 52) as assessed by immunofluorescence.

Analysis:

- Estimand strategy: Secondary Estimand (Section 2.2.2).

- Analysis set: FAS (Section 4) plus data from sibling(s) (Section 2.3.3).
- Analysis methodology: Change from baseline will be analyzed using an ANCOVA model (Section 5.2.1.3) including terms for treatment group, and Screening age covariate (continuous variable).
- Intercurrent events and missing data: All available data in the reporting period will be included during the first 52 weeks. The intercurrent events and missing data will be handled as described in Section 2.2.2
- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and Day 360 (Week 52) for the observed value and change from baseline will be provided for fordadistrogene movaparvovec and placebo.
- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI at Day 360 (Week 52) will be provided.

6.2.2. Serum CK Concentration

Endpoint: Change from Baseline at Week 52 in serum CK concentration

Analysis:

- Estimand strategy: Secondary Estimand (Section 2.2.2).
- Analysis set: FAS (Section 4).
- Analysis methodology: Change from baseline will be analyzed using an MMRM approach for log transformed data (Section 5.2.1.2) including visits through Week 52 where serum CK concentration is assessed (ie, Weeks 1, 2, 5, 9, 13, 18, 35, 52) with additional fixed effects for natural log of Baseline serum CK concentration (continuous variable), Screening age covariate, and natural log of Baseline serum CK concentration by visit interaction, Screening age covariate by visit interaction.
- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.2
- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and all visits through Week 52 where serum CK concentration is assessed for observed serum CK concentration, changes from baseline, and percentage change from baseline will be provided for fordadistrogene movaparvovec and placebo.
- The fordadistrogene movaparvovec and placebo back-transformed LS means (ratio of geometric mean) and 95% CIs along with the back-transformed difference (i.e., ratio)

between the LS means (fordadistrogene movaparvovec – placebo) and the corresponding 95% CIs will be provided for change from Baseline in serum CK concentration for all visits through Week 52 where serum CK concentration is assessed. P-values from the log transformed analysis will be provided.

Graphical displays:

- The distribution of percentage change from Baseline in observed serum CK concentrations for fordadistrogene movaparvovec and placebo at each visit will be displayed graphically using box plots.

- The fordadistrogene movaparvovec and placebo back-transformed LS means and 95% CIs for each visit will be displayed graphically.

6.2.3. Number of Skills Gained and Skills Improved or Maintained based on the NSAA

Endpoints:

- Number of skills gained at Week 52 based on the individual items of the NSAA.

- Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.

6.2.3.1. Main Analysis

- Estimand strategy: Secondary Estimand (Section 2.2.2).

- Analysis set: FAS (Section 4).

- Analysis methodology: For each participant, the number of skills gained at Week 52 will be expressed as a proportion of the number of skills at Baseline that could be gained (numerator is the number of items on NSAA gained at Week 52 and denominator is number of items on NSAA with score 0 at baseline). The number of skills either improved or maintained at Week 52 will be expressed as a proportion of the number of items at Baseline that could be improved or maintained (numerator is the number of items on NSAA improved or maintained at Week 52 and denominator is number of items on NSAA which is 17). These proportions will be analyzed using a generalized mixed linear model with a Binomial distribution and logit link (Section 5.2.3) including terms for treatment group and Screening age covariate (continuous variable).

- Intercurrent events and missing data: All available data at Week 52 will be included. The intercurrent events and missing data will be handled as described in Section 2.2.2

- The number (%) of participants with 0, 1, 2, 3, etc. with skills gained and the number (%) of participants with 0, 1, 2, 3, etc. with skills improved/maintained as observed at Week 52 will be provided for fordadistrogene movaparvovec and placebo. The count of skills gained at Week 52 and count of skills either improved or maintained at Week

52 will be summarized by treatment group using descriptive statistics (including, N, mean, SD, median, Q1, Q3, minimum, and maximum).

Additionally, for the endpoint, number of skills gained, the number of skills that could be gained at Baseline (those with value 0 at Baseline) will be summarized for each treatment group and overall by descriptive statistics (including, N, mean, SD, median, Q1, Q3, minimum, and maximum).

- The fordadistrogene movaparvovec and placebo back-transformed LS means (ie, mean proportion of skills) and 95% CIs along with the back-transformed difference between the LS means (ie, ratio of mean proportions of skills) and 95% CI at Week 52 will be provided. Two-sided p-value will also be provided.

- An estimate of the mean number of skills gained at Week 52, based on the analysis model, can be derived by multiplying the proportion of skills gained (the back-transformed LS Mean) for each treatment group by the mean number of skills at Baseline that could be gained across all participants, irrespective of treatment group.

  An estimate of the mean number of skills improved or maintained at Week 52, based on the analysis model, can be derived by multiplying the proportion of skills improved or maintained (the back-transformed LS Mean) for each treatment group by 17, which is the number of skills at Baseline that could be improved or maintained.

Graphical displays:

- The number (%) of participants with 0, 1, 2, 3, etc. skills gained at Week 52 will be displayed graphically in a bar chart with a bar for each treatment arm. Similarly, the number (%) of participants with 0, 1, 2, 3, etc. skills improved/maintained at Week 52 will be displayed graphically in a bar chart with a bar for each treatment arm.

6.2.3.2. Sensitivity Analysis

This analysis is the same as the main analysis in Section 6.2.3.1 except data from the rater from Clinical Site 1024 with potential data quality issues will be excluded from the analysis.

6.2.4. Rise from Floor and 10 Meter Run/Walk Test

Endpoints:

- Change from Baseline at Week 52 in the 10 meter run/walk test velocity.

- Change from Baseline at Week 52 in the rise from floor velocity.

6.2.4.1. Main Analysis

- Estimand strategy: Secondary Estimand (Section 2.2.2).

- Analysis set: FAS (Section 4).

- Analysis methodology: Change from baseline in velocity will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 where NSAA is assessed (ie, Weeks 9, 18, 35, 52) with additional fixed effects for Baseline velocity (continuous variable), Screening age covariate (continuous variable), Baseline by visit interaction, and Screening age covariate by visit interaction.

- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.2

- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and all visits through Week 52 where NSAA is assessed for observed velocities of the endpoints and changes from baseline in velocity will be provided for fordadistrogene movaparvovec and placebo.

- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from baseline for all visits through Week 52 where NSAA is assessed.

Graphical displays:

- The fordadistrogene movaparvovec and placebo LS means, and 95% CIs for the LS means for each visit will be displayed graphically.

6.2.4.2. Sensitivity Analysis

- This analysis is the same as the main analysis in Section 6.2.4.1 except data from the rater from Clinical Site 1024 with potential data quality issues will be excluded from the analysis.

6.2.5. PODCI Subscales

6.2.5.1. Main Analysis

Endpoints:

- Change from Baseline at Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent)

- Change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent)

Analysis:

- Estimand strategy: Secondary Estimand (Section 2.2.2).

- Analysis set: FAS (Section 4).
- Analysis methodology: Change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 where PODCI is assessed (ie, Weeks 35 and 52) with additional fixed effects for Baseline (continuous variable), Screening age covariate (continuous variable), Baseline by visit interaction, and Screening age covariate by visit interaction.
- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.2
- N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and all visits through Week 52 where PODCI is assessed for observed values and changes from baseline will be provided for fordadistrogene movaparvovec and placebo.
- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from baseline for all visits through Week 52 where PODCI is assessed.

Graphical displays:

- The fordadistrogene movaparvovec and placebo LS means, and 95% CIs for the LS means for each visit will be displayed graphically.

6.2.5.2. Meaningful Within-Patient Change Threshold

eCDF curves of change from Baseline at Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent) and of change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent) will be provided as described in Section 5.4.

6.3. Other Endpoint(s)

None.

6.3.1. Ankle Range of Motion

Endpoint: Change from Baseline at Week 52 in passive ankle range of motion (dorsiflexion).

Analysis:

- Analysis set: FAS (Section 4).
- Analysis methodology: Not applicable.

- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.

- N, mean, SD, median, Q1, Q3, minimum, and maximum for the observed value and change from baseline will be provided for fordadistrogene movaparvovec and placebo by visit and for left ankle and right ankle separately.

6.3.2. Real-life Function Parameters as Assessed by Actigraphy

Endpoint: Change from Baseline at Week 52 in each of the selected parameters assessed by actigraphy:

- Steps per day (steps);

- 95th percentile of cadence (steps/min);

- Median cadence (steps/min);

- Percent time in high activity (%).

Analysis:

- Analysis set: FAS (Section 4).

- Analysis methodology: Change from baseline in each of the selected parameters assessed by actigraphy will be analyzed using a MMRM approach (Section 5.2.1.1) including visits through Week 52 (ie, Weeks 9, 18, 35, 52) with additional fixed effects for Baseline (continuous variable), Screening age covariate (continuous variable), Baseline by visit interaction, and Screening age covariate by visit interaction.

- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.

- N, mean, SD, median, Q1, Q3, minimum, and maximum for the observed value and change from baseline will be provided for fordadistrogene movaparvovec and placebo by visit.

- The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec minus placebo) and the corresponding standard error, two-sided p-value, and 95% CI will be provided for change from baseline for all visits through Week 52 where Real-life Function Parameters are assessed.

Graphical displays:

- The fordadistrogene movaparvovec and placebo LS means, and 95% CIs for the LS means at each visit will be displayed graphically.

6.3.3. Loss of Ambulation

Endpoint: Loss of ambulation through Week 52.

Analysis:

- Analysis set: FAS (through Week 52) (Section 4).
- Analysis methodology: Not applicable.
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- The number (%) of participants with loss of ambulation will be provided for fordadistrogene movaparvovec and placebo. Summary statistics (N, mean, SD, median, Q1, Q3, minimum, and maximum) will be presented for the age of the participant at which loss of ambulation occurs.

6.3.4. Percent Predicted FVC (%pFVC)

Endpoint: Change from Baseline at Week 52 in %pFVC.

- Analysis:
  - Analysis set: FAS (Section 4).
  - Analysis methodology: Change from baseline will be analyzed using an ANCOVA model (Section 5.2.1.3) including terms for treatment group, Baseline %pFVC (continuous variable), and Screening age covariate (continuous variable).
  - Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
  - N, mean, SD, median, Q1, Q3, minimum, and maximum at Baseline and Week 52 for the observed value and change from baseline will be provided for fordadistrogene movaparvovec and placebo.
  - The fordadistrogene movaparvovec and placebo LS means, standard error of each LS mean, and 95% CIs for the LS means along with the difference between the LS means (fordadistrogene movaparvovec – placebo) and the corresponding standard error, two-sided p-value, and 95% CI at Week 52 will be provided.

6.3.5. EQ-5D-Y Assessment

Endpoint: Response to each of the 5 dimensions at Week 52 on the EQ-5D-Y proxy assessment at Week 52.

Analysis:

- Analysis set: FAS (Section 4).
- Analysis methodology: Not applicable.
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- For each of the 5 dimensions, the number and percent of participants responding as 'no problems', 'some problems', or 'a lot of problems' will be provided for fordadistrogene movaparvovec and placebo.
- For each of the 5 dimensions, change from baseline to Week 52 will be summarized using shift tables for fordadistrogene movaparvovec and placebo.

Endpoint: Change from Baseline at Week 52 on the EQ VAS proxy assessment.

Analysis:

- Analysis set: FAS (Section 4).
- Analysis methodology: Not applicable.
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- N, mean, SD, median, Q1, Q3, minimum, and maximum for the observed value and change from baseline will be provided for fordadistrogene movaparvovec and placebo.

6.3.6. QoL of Caregivers of Participants

If a participant changes his caregiver during the reporting period, from the one at baseline, all values collected after the change will be set to missing.

Endpoint:

- Response to each of the 5 dimensions of the EQ-5D-5L assessment at Week 52 (caregivers of participants).

Analysis:

- Analysis set: Caregivers of participants in the FAS (Section 4). Caregivers of siblings will be included in the analyses only once.
- Analysis methodology: Not applicable
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- For each of the 5 dimensions, the number and percent of caregivers of participants responding as 'no problems', 'slight problems', 'moderate problems', 'severe problems', or 'unable to/extreme problems' will be provided at Baseline and Week 52 for fordadistrogene movaparvovec and placebo.
- For each of the 5 dimensions, change in response from baseline at Week 52 will be summarized using shift tables for fordadistrogene movaparvovec and placebo.

Endpoints:

- Change from baseline at Week 52 in the EQ-5D-5L VAS assessment (caregivers of participants)
- Change from baseline at Week 52 in the EQ-5D-5L index score (caregivers of participants)

Analysis:

- Analysis set: Caregivers of participants in the All Randomized (Section 4). Caregivers of siblings will be included in the analyses only once.
- Analysis methodology: Not applicable
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- For each participant's caregiver at baseline, N, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and at Week 52 for observed values and changes from baseline will be provided for fordadistrogene movaparvovec and placebo.
- If more than 5 participants change their caregivers from the ones at baseline during the reporting period, N, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and all visits through Week 78 where EQ-5D-5L is assessed for caregivers for observed values will be provided for fordadistrogene movaparvovec and placebo by visit.

6.3.7. Immune Response to Dystrophin/Mini-dystrophin and to AAV9

Endpoints:

- Immune response: ADA and T cell response to mini-dystrophin transgene protein
- Immune response: ADA, NAb and T cell response to AAV9 capsid

Analysis:

- Analysis set: Safety Analysis Set (through Week 52) (Section 4).
- Analysis methodology: Not applicable.
- Missing data: All available data in the reporting period will be included. Missing data will not be imputed.
- The number and percent of participants who are (1) ADA-positive to mini-dystrophin transgene protein, (2) T cell response-positive to mini-dystrophin transgene protein by peptide pool (3) ADA-positive to AAV9, (4) NAb-positive to AAV9, and (5) T cell response-positive to AAV9 by peptide pool will be provided by visit, and an overall number and percent of participants who are positive at any post-screening visit for fordadistrogene movaparvovec and placebo.
- The observed titers for ADA-positive to mini-dystrophin participants, ADA-positive to AAV9 participants and NAb-positive to AAV9 participants will be summarized (N, mean, SD, median, Q1, Q3, minimum, and maximum) by visit for fordadistrogene movaparvovec and placebo.
- The observed levels for participants who have positive T cell response to mini-dystrophin transgene protein and T cell response to AAV9 will be summarized (N, mean, SD, median, Q1, Q3, minimum, and maximum) by peptide pool and visit for fordadistrogene movaparvovec and placebo.
- Analysis windows for these summaries are provided in Appendix 2.1, Note that unplanned visits will be included in the overall summaries only.
- Listings of the positive/negative status and associated observed titers/observed levels for the immunogenicity endpoints listed above by visit for fordadistrogene movaparvovec and placebo.

Graphical display:

- Box-plots for observed titers for ADA-positive and NAb-positive participants will be presented by visit for fordadistrogene movaparvovec and placebo.
- Box-plots for observed levels for participants with positive T cell response to mini-dystrophin transgene protein and positive T cell response to AAV9 capsid will be presented by peptide pool and visit for fordadistrogene movaparvovec and placebo.

6.3.8. Viral Vector Shedding

Samples collected for viral vector shedding are only assayed for Cohort 1 (initially fordadistrogene movaparvovec) participants.

Note that there may be participants for which sample collection may continue after 2 consecutive undetectable samples because notification to stop may be provided after the participant has had another scheduled visit where a sample was to be collected or a site may mistakenly collect a sample after receiving notification to stop sample collection.

Endpoint:

- Peak viral vector levels (vg/ml) post fordadistrogene movaparvovec administration for each of the five profiles – one without MNase treatment for whole blood, one without MNase for saliva, one with MNase for saliva, one without MNase for urine, one with MNase for urine

Analysis:

- Analysis set: Viral Vector Shedding subset of Safety Analysis Set (through Week 52) (Section 4).
- Analysis methodology: Not applicable.
- Missing data: Missing/undetectable results will not be imputed.
- N, mean, SD, median, Q1, Q3, minimum, and maximum will be provided .

Endpoint:

- Time in weeks of peak viral vector shedding post fordadistrogene movaparvovec administration for each of the five profiles – one without MNase treatment for whole blood, one without MNase for saliva, one with MNase for saliva, one without MNase for urine, one with MNase for urine

Analysis:

- Analysis set: Viral Vector Shedding subset of Safety Analysis Set (through Week 52) (Section 4).
- Analysis methodology: Not applicable.
- Missing data: Missing/undetectable results will not be imputed.
- N, mean, SD, median, Q1, Q3, minimum, and maximum will be provided.

Endpoint:

- Time in weeks to undetectable viral vector (time to clearance of viral vector) from date of fordadistrogene movaparvovec administration for each of the five profiles – one without MNase treatment for whole blood, one without MNase for saliva, one with MNase for saliva, one without MNase for urine, one with MNase for urine.

- Time in weeks to the last undetectable viral vector from date of fordadistrogene movaparvovec administration for each of the five profiles – one for whole blood, two for saliva, two for urine.

Analysis:

- Analysis set: Viral Vector Shedding subset of Safety Analysis Set (through Week 52) (Section 4).

- Analysis methodology: Time in weeks to undetectable viral vector and last undetectable viral vector will be summarized using the K-M method (Section 5.2.2). The 25th, 50th and 75th percentile of time to undetectable viral vector and last undetectable viral vector will be provided along with 95% confidence intervals based on the Breslow-Day method. The range will also be presented.

- Missing data: Missing/undetectable results will not be imputed.

Graphical displays:

- Kaplan-Meier plots of time to undetectable viral vector and time to the last undetectable viral vector for each of the five profiles – one without MNase treatment for whole blood, one without MNase for saliva, one with MNase for saliva, one without MNase for urine, one with MNase for urine

6.4. Global Statistical Test

The following endpoints will be included in the GST and will be considered as an exploratory analysis. The number of skills gained and number of skills improved or maintained will not be included in the GST as they are derived from the same 17 individual NSAA skills that contributed to the NSAA total score.

- Change from Baseline at Week 52 in the NSAA total score.

- Change from Baseline at Week 52 in the 10 meter run/walk test velocity.

- Change from Baseline at Week 52 in the rise from floor velocity.

- Change from Baseline at Week 52 in the 95th percentile of cadence.

Analysis set: FAS (Section 4).

- Analysis methodology: The GST will be conducted as described in Section 5.2.4 by combining summary statistics for select functional endpoints listed above into a single global test statistic.

- For each endpoint, the estimated group difference from MMRM, the corresponding standard error, and standardized z score will be provided. The mean observed z score across multiple endpoints, and p-value for the GST will be provided.

6.5. Subset Analyses

Subgroup analyses based on Screening age strata, Baseline NSAA Total score, and Geographic region strata will be performed for primary efficacy endpoint and the select secondary efficacy endpoints.

6.5.1. Screening Age Strata

The following endpoints will be evaluated by two screening age strata (<6 years and ≥ 6 years):

- Change from Baseline at Week 52 in the NSAA total score.

- Change from Baseline at Week 52 in the 10 meter run/walk test velocity.

- Change from Baseline at Week 52 in the rise from floor velocity.

- Number of skills gained at Week 52 based on the individual items of the NSAA.

- Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.

- Change from Baseline at Week 52 in the 95th percentile of cadence.

The age strata at screening (Randomization Group) collected in the clinical database will be used for subset analysis.

- Analysis set: FAS (Section 4).

- Analysis methodology:

- The analysis methods for the main analysis of primary endpoint in Section 6.1 and the secondary endpoints in Section 6.2 will be applied for the subset analysis, where the model will be handled in a different way as below:

    1. Analysis for the endpoints change from Baseline at Week 52 in the NSAA total score, 10 meter run/walk test velocity, rise from floor velocity, and 95th percentile of cadence.

- For each Screening age strata separately, change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 with additional fixed effects for Baseline(continuous variable), and Baseline by visit interaction.

  For each Screening age strata, estimates of the mean changes from Baseline, standard error of each LS mean, and 95% confidence intervals for fordadistrogene movaparvovec and placebo will be provided for each visit along with the mean treatment group difference and the corresponding standard error, two-sided p-value, and two-sided 95% confidence interval for the mean difference at each visit.

- Change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including visits through Week 52 with additional fixed effects for Baseline (continuous variable), Baseline by visit interaction, Screening age strata (binary variable), Screening age strata by visit interaction, and Screening age strata by treatment group interaction.

  The p-value for the Screening age strata interaction term will be provided.

2. Analysis for endpoints number of skills gained and number of skills either improved or maintained at Week 52

   - For each subset separately, the number of skills will be analyzed using the approach described in Section 5.2.3.

   - For each subset, estimates of the LS means and 95% confidence intervals for fordadistrogene movaparvovec and placebo will be provided along with the difference in LS means and corresponding standard error, two-sided p-value, and two-sided 95% confidence interval for the mean difference.

   - The number of skills will be analyzed using the approach described in Section 5.2.3 with fixed effects for Screening age strata (categorical variable) instead of age model covariate, and Screening age strata by treatment group interaction. The p-value for the Screening age strata by treatment group interaction term will be provided.

- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.1 and Section 2.2.2 accordingly.

- For each Screening age strata separately, the summary for each endpoint will be performed the same way as described in the corresponding main analysis in Section 6.1 and Section 6.2.

6.5.2. Baseline NSAA Total score

The following endpoints will be evaluated by Baseline NSAA total score strata:

- Change from Baseline at Week 52 in the NSAA total score
- Change from Baseline at Week 52 in the 10 meter run/walk test velocity.
- Change from Baseline at Week 52 in the rise from floor velocity.

- Baseline NSAA total score strata will be defined by the observed median of baseline NSAA total score based on all participants in the FAS during the reporting period. The 2 subgroups will be determined as below:

1. < Median
2. ≥ Median

Analysis:

- Analysis set: FAS (Section 4).
- Analysis methodology:

  For each baseline NSAA total score strata separately, change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including fixed effects for treatment group (categorical variable), visit (ordered categorical variable), and treatment group by visit interaction with additional fixed effects for screening age covariate (continuous variable) and screening age by visit interaction.

  For each baseline NSAA total score strata, estimates of the mean changes from Baseline, standard error of each LS mean, and 95% confidence intervals for fordadistrogene movaparvovec and placebo will be provided for each visit along with the mean treatment group difference and the corresponding standard error, two-sided p-value, and two-sided 95% confidence interval for the mean difference at each visit.

- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.1 and Section 2.2.2 accordingly.
- For each baseline NSAA total score strata separately, the summary for each endpoint will be performed the same way as described in the corresponding main analysis in Section 6.1 and Section 6.2.

6.5.3. Geographic Region

The following endpoints will be evaluated by geographic regions:

- Change from Baseline at Week 52 in the NSAA total score
- Change from Baseline at Week 52 in the 10 meter run/walk test velocity.
- Change from Baseline at Week 52 in the rise from floor velocity.

The geographic regions in this study will be categorized as North America, Europe, and Asia-Pacific.

Analysis:

- Analysis set: FAS (Section 4).
- Analysis methodology:

  For each geographic region strata separately, change from baseline will be analyzed using an MMRM approach (Section 5.2.1.1) including fixed effects for treatment group (categorical variable), visit (ordered categorical variable), and treatment group by visit interaction with additional fixed effects for baseline (continuous variable) and baseline by visit interaction, with additional fixed effects for screening age covariate (continuous variable) and screening age by visit interaction

  For each geographic region strata, estimates of the mean changes from Baseline, standard error of each LS mean, and 95% confidence intervals for fordadistrogene movaparvovec and placebo will be provided for each visit along with the mean treatment group difference and the corresponding standard error two-sided p-value, and two-sided 95% confidence interval for the mean difference at each visit.

- Intercurrent events and missing data: All available data in the reporting period will be included. The intercurrent events and missing data will be handled as described in Section 2.2.1 and Section 2.2.2 accordingly.
- For each geographic region strata separately, the summary for each endpoint will be performed the same way as described in the corresponding main analysis in Section 6.1 and Section 6.2. No plots will be produced for these analyses.

6.6. Baseline and Other Summaries and Analyses

6.6.1. Baseline Summaries

All summaries will be performed for the Safety Analysis Set population. Demographic and baseline characteristics will also be performed for the FAS populations.

1. Demographic characteristics will be summarized. Age categories to display are ≥4 to <5 years, ≥5 to <6 years, ≥6 to < 7 years, and ≥7 to < 8 years.

2. Screening age strata (< 6 years and ≥ 6 years old) will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups using number and percent of participants.

3. Baseline physical measurements (including height and weight) will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups.

4. The below will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups using number and percent of participants:

   - DMD genetic results.
   - Enrollment geographical region and country.

5. Background glucocorticoid regimen will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups. Prednisolone and prednisone will be combined for this analysis. The number and percent of participants for each glucocorticoid being received at Screening will be presented. Descriptive statistics (N, mean, SD, median, Q1, Q3, minimum and maximum) will be presented for

   - Daily dose (mg/kg) for each glucocorticoid the participant is receiving at Screening.
   - Duration of glucocorticoid use (months) for glucocorticoid dose the participant is receiving at Screening.
   - Age at initiation of any glucocorticoid use.

6. General medical history will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups.

7. Prior medications will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups.

8. Study inclusion and exclusion criteria at Screening will be summarized for screen failures. IP administration eligibility will be summarized by randomized treatment assignment (ie, fordadistrogene movaparvovec and placebo) for participants who were randomized but not treated.

9. The below will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups using descriptive statistics (N, mean, SD, median, Q1, Q3, minimum, and maximum):

   - Baseline NSAA total score.
   - Screening age (years) covariate.
   - Age (years) at dosing with IP on Year 1 Day 1.

6.6.2. Study Conduct and Participant Disposition

1. The below participant populations/sets will be summarized for fordadistrogene movaparvovec and placebo and for combined treatment groups.

   - Enrolled.
   - Randomly assigned to investigational product.
   - Treated.
   - Full Analysis Set.
   - Safety Analysis Set (through Week 52).
   - Biceps Brachii Muscle Biopsies
   - Viral Vector Shedding Kinetics

2. Participant disposition (eg, discontinuation from study, reason for discontinuation, completed study, and ongoing) will be summarized for fordadistrogene movaparvovec and placebo.

3. Medication errors will be listed.

4. Important protocol deviations will be summarized.

6.6.3. Study Treatment Exposure

The actual administered dose of fordadistrogene movaparvovec in vg and vg/kg will be summarized (n, mean, SD, median, Q1, Q3, minimum and maximum) for Year 1 Day 1 in the Safety Analysis Set (through Week 52) (Section 4). The percent of planned volume of IP administered will be categorized as 0% to ≤25%, >25% to ≤50%, >50% to ≤75%, and >75% for fordadistrogene movaparvovec and placebo.

6.6.4. Concomitant Medications

The World Health Organization (WHO)-Drug coding dictionary will be used to classify concomitant medications.

The number and percent of participants who took each concomitant medication will be provided for fordadistrogene movaparvovec and placebo in the Safety Analysis Set (through Week 52) (Section 4).

6.7. Safety Summaries and Analyses

All analyses will be performed for the Safety Analysis Set (through Week 52).

6.7.1. Adverse Events

Incidence of TEAEs (all-causality and treatment-related) in the reporting period will be summarized by SOC, PT, and severity for fordadistrogene movaparvovec and placebo. Adverse events may be clustered to reflect medical concepts.

A summary of the TEAEs (all-causality and treatment-related) occurring during the reporting period will be tabulated by PT sorted by decreasing incidence for fordadistrogene movaparvovec and placebo. The most commonly reported TEAEs will be summarized using those PTs with high frequency (cutoff depends on the final frequency of TEAEs) for fordadistrogene movaparvovec-dosed participants in the safety analysis set.

Deaths and SAEs will be listed and incidence of SAEs(all causality and treatment-related) will be summarized by SOC and PT for fordadistrogene movaparvovec and placebo.

A summary of the SAEs (all-causality and treatment-related) occurring during the reporting period will be tabulated by PT sorted by decreasing incidence for fordadistrogene movaparvovec and placebo. The most commonly reported SAEswill be summarized using those PTs with high frequency (cutoff depends on the final frequency of serious TEAEs) for fordadistrogene movaparvovec-dosed participants in the safety analysis set.

For each participant who reported a TEAE (all-causality or onset treatment-related), the time (in days) to (date of onset of the event - date of dosing + 1) for that TEAE will be summarized by PT as continuous data. Participants with multiple TEAEs will be included multiple times in the summary statistics. Events that occur on the day of dosing will have a time of onset as day 1.

For each participant who reported a serious TEAE (all-causality or treatment-related), the time (in days) to onset (date of onset of the event - date of dosing + 1) for that serious TEAE will be summarized by PT as continuous data. Participants with multiple serious TEAEs will be included multiple times in the summary statistics. Events that occur on the day of dosing will have a time of onset as Day 1.

Adverse events of interest will be summarized using incidence of all-causality AEs (by severity) and SAEs (across all severities). Several PTs would be combined as cluster terms, and incidence for both component PTs and cluster terms will be included. Cluster categories and PTs with “Peri infusion” will include AEs of interest with an onset in the first 2 weeks after dosing (Day 1 through Day 14) while “Late Onset” will include AEs of interest with an onset date after week 4 (Week 5 or later). The final list of AEs of interest will be maintained in a separate document and finalized before the database release.

Onset of AEs of interest (all-causality) will be summarized by intervals. The interval is defined as the number of weeks rounded to next highest integer from the fordadistrogene movaparvovec or placebo administration to the earliest of date of AE of interest or date of data cut-off (i.e., [end date – dosing date +1]/7 for weeks. The total duration of follow up for each participant is relative to death/study discontinuation/or data cut-off. For example, week 1 is for days 1-7 and week 2 is for days 8-14).

For each duration of follow-up interval, total number of AEs of interest that occur during an interval will contribute to the numerator of the percentage. Total count of AEs of interest that occur in the entire reporting period will contribute to the denominator of the percentage. Day 390 or one day prior to Year 2 dosing will be considered as having follow-up up to 52 weeks.

The AEs of interest for both cluster terms and the component PTs will be summarized by interval durations in weeks. For these AEs of interest cluster terms and the components PTs, duration of the adverse events will be summarized descriptively (N, mean, SD, median, Q1, Q3, minimum, and maximum). Participants with multiple AEs of interest will be included multiple times in the summary statistics.

6.7.2. Laboratory Data

Central and local laboratory test results will be combined for reporting purposes.

Incidence of laboratory test abnormalities will be summarized for fordadistrogene movaparvovec and placebo without regard to baseline abnormality, for normal baseline, and for abnormal baseline. If there is a local and central laboratory collection on the same day, both values will be considered for analysis.

For select laboratory test parameters, data will be summarized and displayed graphically as described below;

	Presentation		
Parameter	**Table: Changes and % changes from baseline By visit**	**Shift table: <LLN, normal, >ULN By visit**	**Graph: Box-plot**
GLDH	X	X[a]	X (observed values)
CK	X		X[f]
GGT	X	X[b]	X (observed values)
C3 and C4	X		X (observed values)
Platelets	X	X[c]	X (observed values)
Creatinine	X		X (observed values)
cTn-I	X[d] (observed values)	X[e]	X[f] (observed values)

a. ≥2xULN and <3xULN, ≥3xULN and <4xULN, and ≥4xULN will be applied in shift table

b. >ULN -and ≤2.5 x ULN, > 2.5 and ≤5.0 x ULN , >5.0 and ≤20.0 x ULN, >20.0 x ULN will be applied in shift table

c. ≥75 and <LLN, ≥50 and <75, ≥25 and <50, and <25 and will be applied in shift table (in $10^3/mm^3$)

d. The ratio cTn-I/ULN will be used in the shift table

e. cTn-I/ULN ratio ≥3 - <10, ≥10 - <100, ≥100

f. Spaghetti plot of % change from baseline in CK and ratio cTn-I/ULN will be generated

1. CK, GLDH, GGT:

   - Changes and percent changes from baseline will be summarized descriptively in tabular format for fordadistrogene movaparvovec and placebo by visit. Observed values will be displayed graphically using box plots for fordadistrogene movaparvovec and placebo by visit.

     Changes from baseline for GGT and GLDH will also be summarized using shift tables for fordadistrogene movaparvovec and placebo. The shift table will use baseline values categorized as >ULN -and ≤2.5 x ULN, >2.5 and ≤5.0 x ULN, >5.0 and ≤ 20.0 x ULN, >20.0 x ULN) for GGT, and ≥2xULN and <3xULN, ≥3xULN and <4xULN, and ≥4xULN for GLDH, respectively.

2. C3, C4, Platelets, Creatinine:

   - Observed values will be summarized descriptively in tabular format for fordadistrogene movaparvovec and placebo by visit.

   - Observed values for platelets will also be summarized using shift tables for fordadistrogene movaparvovec and placebo. The shift table will use baseline values categorized as ≥75 and <LLN, ≥50 and <75, ≥25 and <50, and <25.

   - Observed values will be displayed graphically using box plots for fordadistrogene movaparvovec and placebo by visit.

3. For cTn-I:

   For each of the treatments fordadistrogene movaparvovec and placebo, the participants will be divided into two categories: those with baseline cTn-I ≤99th percentile (ie. ULN) and those with baseline cTn-I >99th percentile (ie. ULN). For Centaur assay, the cTn-I 99th percentile (ie. ULN) will be 0.03 ng/ml. The LLoQ is 0.03 and values below LLoQ will set to 0.029. For the Beckman assay, the cTn-I 99th percentile (ie. ULN) will be 19.8 ng/L. The LLoQ is 2.3 ng/L and values below LLoQ will set to 2.29 ng/L. The number and percent of participants in each category by fordadistrogene movaparvovec and placebo will be presented.

   For participants at sites where local cTn-I cannot be measured at the Baseline visit, the baseline cTn-I value (last value prior to the IP administration) will be from Screening visit as assessed by the central laboratory.

   The observed cTn-I value will be normalized using ULN from the corresponding visit and the ratio of cTn-I/ULN will be summarized descriptively (mean, SD, median, Q1, Q3, minimum and maximum).

- Spaghetti plot of the ratio cTn-I/ULN including all participants for each treatment group will be generated. Color pattern will be used for participants with ≥ 2 consecutive visit assessments post-baseline that are >3xULN.

All visits (ie, planned and unplanned) will be included in these analyses.

Analysis windows for these summaries and graphical displays by visit are provided in Appendix 2.1.

To assess liver injury, a listing of the participants potentially meeting Hy's Law criteria and E-DISH plots will be produced.

The parameters International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M, Hepatitis B surface antigen, and Hepatitis C antibody will be listed only as they are only collected to assess study entry criteria.

6.7.3. Vital Signs (including body weight)

Observed values and changes from baseline in vital sign parameters will be summarized descriptively for fordadistrogene movaparvovec and placebo by visit. If there are multiple records at any timepoint after the start of infusion on Day 1, the average will be included in the analysis.

Categorical tables including post-baseline values, maximum increases (in blood pressure and pulse rate), and maximum decreases (in blood pressure and pulse rate) will be provided. Additionally, categorical tables will also be provided for the first 7 days of follow-up and the first 30 days of follow-up.

6.7.4. Electrocardiograms

Changes from baseline (QT interval, heart rate, QTcF, PR interval, and QRS complex) in ECG parameters will be summarized descriptively for fordadistrogene movaparvovec and placebo by visit. Additionally, the number (%) of participants with ECG findings of potential clinical concern as defined in Appendix 2.2.2 will be summarized for fordadistrogene movaparvovec and placebo.

6.7.5. Physical Examination and Neurological Examinations

No specific data summaries will be provided for physical or neurological examinations. Any findings considered by the investigator to be 'clinically significant' will be recorded as adverse events and will be included in the adverse event summaries.

6.7.6. Echocardiograms

- Changes from baseline to last observation in echocardiogram parameters will be summarized descriptively for continuous parameters and as number and percent of participants for binary parameters for fordadistrogene movaparvovec and placebo.

6.7.7. Cardiac MRI

Observed values and changes from baseline to last observation in cardiac MRI parameters will be summarized descriptively for fordadistrogene movaparvovec and placebo.

6.7.8. Child Behavior Check List (CBCL)

Number and percentage of participants will be presented for each of the following variables for fordadistrogene movaparvovec and placebo:

- Withdrawn T-score or Withdrawn/Depressed Syndrome T-Score ≥65;
- Internalizing Global Scale T-Score ≥60.

7. INTERIM ANALYSES

There are 2 options for interim analyses, both of which are designed to provide data to support an earlier regulatory submission for BLA/MAA based on the primary endpoint of change from Baseline at Week 52 in the NSAA total score. The objective of each interim analysis is to demonstrate a statistically significant effect of fordadistrogene movaparvovec on the primary endpoint of change from Baseline at Week 52 in the NSAA total score compared to placebo. Additionally, an assessment of futility (non-binding) based on the primary endpoint will be made at each interim analysis, if performed.

The first interim analysis may be performed when approximately 30 participants in the FAS have completed visits through Week 52, and the second interim may be performed when approximately 60 participants in the FAS have completed visits through Week 52. The decision to conduct either interim analysis will be based on regulatory feedback, study recruitment rates and emerging data from other studies in the program. The objectives, estimands, endpoints, and analysis method for each interim analysis are identical to the main analysis (Section 6.1.1). If either interim analysis is performed, a group sequential approach will be applied to the efficacy analyses to control Type I error rate across the interim analysis/analyses and the primary analysis. Specifically, a gamma family alpha-spending function with gamma parameter -1 will be used. Additionally, an assessment of futility (non-binding) based on the primary endpoint will be made at each interim analysis, if performed, using a gamma family spending function with gamma parameter -4.

The statistical analyses planned for these two IAs will be detailed in a separate IA SAP.

8. REFERENCES

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9. APPENDICES

Appendix 1. Summary of Efficacy Analyses

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
NSAA total score				
Change from Baseline at Week 52 in the NSAA total score	Summary eCDF curves	FAS	All available data will be included Missing data will not be imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the NSAA total score	Main analysis Plot of LS means and 95% CIs	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline NSAA total score, Screening age covariate, Baseline NSAA total score by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the NSAA total score	Sensitivity	FAS	All available data will be included Missing data will be imputed using copy increments in reference approach	ANCOVA with covariates for Baseline NSAA total score and Screening age.
Change from Baseline at Week 52 in the NSAA total score	Sensitivity	FAS	All available data will be included Tipping point analysis to assess missing data	ANCOVA with covariates for Baseline NSAA total score and Screening age.
Change from Baseline at Week 52 in the NSAA total score	Sensitivity	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline NSAA total score, Screening age covariate, Baseline NSAA total score by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the NSAA total score	Sensitivity #4	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline NSAA total score, dosing age covariate, Baseline NSAA total score by visit interaction, and dosing age covariate by visit interaction

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the NSAA total score	Summary	FAS	All available data will be included Missing data will not be imputed	Not applicable (N/A) Plot and descriptive statistics will use dosing age
Change from Baseline at Week 52 in the NSAA total score	Supplementary	FAS plus siblings	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline NSAA total score, Screening age covariate, Baseline NSAA total score by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the NSAA total score	Screening age strata subset Summary	FAS	All available data will be included Missing data will not be imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the NSAA total score	Screening age strata subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each Screening age strata separately, MMRM with additional fixed effects for Baseline NSAA total score, and Baseline NSAA total score by visit interaction.
Change from Baseline at Week 52 in the NSAA total score	Screening age strata subset The p-value for the Screening age strata interaction term	FAS	All available data will be included Missing data will not be explicitly imputed	NSAA main analysis (MMRM) subset on Screening age strata and MMRM with additional fixed effects for Baseline NSAA total score, Baseline NSAA total score by visit interaction, Screening age strata, Screening age strata by visit interaction, and Screening age strata by treatment group interaction.
Change from Baseline at Week 52 in the NSAA total score	Baseline NSAA total score subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the NSAA total score	Baseline NSAA total score subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each baseline NSAA total score strata separately, MMRM with fixed effects for treatment group, visit, and treatment group by visit interaction with additional fixed effects for screening age covariate and screening age by visit interaction.
Change from Baseline at Week 52 in the NSAA total score	Geographic region subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the NSAA total score	Geographic region subset	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with treatment group, visit, and treatment group by visit interaction with additional fixed effects for baseline, baseline by visit interaction, screening age covariate, and screening age by visit interaction
Muscle Biopsies				
Change from Baseline in percent normal mini-dystrophin expression level at Day 360 (Week 52)	Summary Box plots	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline in percent normal mini-dystrophin expression level at Day 360 (Week 52)	Main analysis	FAS	All available data will be included Missing data will not be imputed	ANCOVA with additional terms for Baseline and Screening age covariate

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline in percent normal mini-dystrophin expression level at Day 360 (Week 52)	Supplementary	FAS plus siblings	All available data will be included Missing data will not be imputed	ANCOVA with additional terms for Baseline and Screening age covariate
Change from Baseline in percent of muscle fibers expressing mini-dystrophin at Day 360 (Week 52)	Summary Box plots	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline in percent of muscle fibers expressing mini-dystrophin at Day 360 (Week 52)	Main analysis	FAS	All available data will be included Missing data will not be imputed	ANCOVA with additional terms for Baseline and Screening age covariate
Change from Baseline in percent of muscle fibers expressing mini-dystrophin at Day 360 (Week 52)	Supplementary	FAS plus siblings	All available data will be included Missing data will not be imputed	ANCOVA with additional terms for Baseline and Screening age covariate
CK				
Change from Baseline at Week 52 in serum CK concentration	Summary (observed, change from baseline, and percentage change from baseline) Box plots (percent change from Baseline)	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in serum CK concentration	Main analysis Plot of back-transformed LS means and 95% CIs	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM log transformed data with additional fixed effects for natural log of Baseline, Screening age covariate, natural log of Baseline by visit interaction, and Screening age covariate by visit interaction Back-transformed LSmeans, difference and 95%CI.

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
NSAA Skills				
Number of skills gained at Week 52	Summary Bar chart	FAS	All available data will be included Missing data will not be imputed	N/A
Number of skills gained at Week 52	Main analysis	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills gained at Week 52	Summary Bar chart	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	N/A
Number of skills gained at Week 52	Sensitivity analysis	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills gained at Week 52	Screening age strata subset	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills gained at Week 52	Screening age strata subset The p-value for Screening age strata interaction term	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with Screening age strata (categorical variable), and Screening age strata by treatment group interaction
Number of skills either improved or maintained at Week 52	Summary Bar chart	FAS	All available data will be included Missing data will not be imputed	N/A

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Number of skills either improved or maintained at Week 52	Main analysis	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills either improved or maintained at Week 52	Summary Bar chart	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	N/A
Number of skills either improved or maintained at Week 52	Sensitivity analysis	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills either improved or maintained at Week 52	Screening age strata subset	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with an additional term for Screening age covariate Back-transformed LS means, difference and 95%CI
Number of skills either improved or maintained at Week 52	Screening age strata subset The p-value for Screening age strata interaction term	FAS	All available data will be included Missing data will not be imputed	Generalized linear model with binomial distribution and logit link and with Screening age strata (categorical variable), and Screening age strata by treatment group interaction
NSAA timed tests				
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Main analysis Plot of LS means and 95% CIs	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Summary	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Sensitivity analysis Plot of LS means and 95% CIs	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Screening age strata subset Summary	FAS	All available data will be included Missing data will not be imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Screening age strata subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each Screening age strata separately, MMRM with additional fixed effects for Baseline NSAA total score, and Baseline NSAA total score by visit interaction.
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Screening age strata subset The p-value for the Screening age strata interaction term	FAS	All available data will be included Missing data will not be explicitly imputed	NSAA main analysis (MMRM) subset on Screening age strata and MMRM with additional fixed effects for Baseline NSAA total score, Baseline NSAA total score by visit interaction, Screening age strata, Screening age strata by visit interaction, and Screening age strata by treatment group interaction.
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Baseline NSAA total score subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Baseline NSAA total score subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each baseline NSAA total score strata separately, MMRM with fixed effects for treatment group, visit, and treatment group by visit interaction with additional fixed effects for screening age covariate and screening age by visit interaction.
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Geographic region subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the 10 meter run/walk velocity	Geographic region subset	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with treatment group, visit, and treatment group by visit interaction with additional fixed effects for baseline, baseline by visit interaction, screening age covariate, and screening age by visit interaction
Change from Baseline at Week 52 in the rise from floor velocity	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in the rise from floor velocity	Main analysis Plot of LS means and 95% CIs	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the rise from floor velocity	Summary	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be imputed	N/A

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the rise from floor velocity	Sensitivity analysis	FAS	All available data excluding the data from the particular rater(s) with potential data quality issues will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the rise from floor velocity	Screening age strata subset Summary	FAS	All available data will be included Missing data will not be imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the rise from floor velocity	Screening age strata subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each Screening age strata separately, MMRM with additional fixed effects for Baseline, and Baseline by visit interaction.
Change from Baseline at Week 52 in the rise from floor velocity	Screening age strata subset The p-value for the Screening age strata interaction term	FAS	All available data will be included Missing data will not be explicitly imputed	NSAA main analysis (MMRM) subset on Screening age strata and MMRM with additional fixed effects for Baseline , Baseline by visit interaction, Screening age strata, Screening age strata by visit interaction, and Screening age strata by treatment group interaction.
Change from Baseline at Week 52 in the rise from floor velocity	Baseline NSAA total score subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the rise from floor velocity	Baseline NSAA total score subset	FAS	All available data will be included Missing data will not be explicitly imputed	For each baseline NSAA total score strata separately, MMRM with fixed effects for treatment group, visit, and treatment group by visit interaction with additional fixed effects for screening age covariate and screening age by visit interaction.

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Change from Baseline at Week 52 in the rise from floor velocity	Geographic region subset Summary	FAS	All available data will be included Missing data will not be explicitly imputed	Not applicable (N/A)
Change from Baseline at Week 52 in the rise from floor velocity	Geographic region subset	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with treatment group, visit, and treatment group by visit interaction with additional fixed effects for baseline, baseline by visit interaction, screening age covariate, and screening age by visit interaction
PODCI				
Change from Baseline at Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent)	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent)	Main analysis Plot of LS means and 95% CIs	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent)	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent)	Main analysis Plot of LS means and 95% CIs eCDF curves	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Ankle Range of Motion				
Change from Baseline at Week 52 in passive ankle range of motion (dorsiflexion)	Summary for left and right ankle separately	FAS	All available data will be included Missing data will not be imputed	N/A
Actigraphy				
Change from Baseline at Week 52 in real-life function parameters as assessed by actigraphy	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in real-life function parameters as assessed by actigraphy	Main analysis Plot of LS means and 95% CI for each LS mean	FAS	All available data will be included Missing data will not be explicitly imputed	MMRM with additional fixed effects for Baseline, Screening age covariate, Baseline by visit interaction, and Screening age covariate by visit interaction
Change from Baseline at Week 52 in 95th percentile of cadence	Screening age strata subset The p-value for the Screening age strata interaction term	FAS	All available data will be included Missing data will not be explicitly imputed	NSAA main analysis (MMRM) subset on Screening age strata and MMRM with additional fixed effects for Baseline, Baseline by visit interaction, Screening age strata, Screening age strata by visit interaction, and Screening age strata by treatment group interaction.
Global Statistical Test				

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
• Change from Baseline at Week 52 in the NSAA total score. • Change from Baseline at Week 52 in the 10 meter run/walk test velocity. • Change from Baseline at Week 52 in the rise from floor velocity. • Change from Baseline at Week 52 in the 95th percentile of cadence.	Exploratory analysis	FAS	All available data will be included Missing data will not be imputed	Standardized z score will be obtained from the estimated group difference by MMRM for each endpoint, the mean z score will be calculated across the select multiple endpoints. The p value for the global statistical test will be estimated by permutation.
Loss of ambulation				
Loss of ambulation through Week 52	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
%pFVC				
Change from Baseline at Week 52 in %pFVC	Summary	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 in %pFVC	Main analysis	FAS	All available data will be included Missing data will not be imputed	ANCOVA with additional terms for Baseline and Screening age covariate
EQ-5D-Y				
Response to each of the 5 dimensions on the EQ-5D-Y proxy assessment at Week 52	Summary Shift table	FAS	All available data will be included Missing data will not be imputed	N/A
Change from Baseline at Week 52 on the EQ VAS proxy assessment	Summary	FAS	All available data will be included Missing data will not be imputed	N/A

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
QoL of Caregivers of Participants				
Response to each of the 5 dimensions of the EQ-5D-5L assessment at Week 52 (caregivers of participants)	Summary Shift table	Caregivers of participants in the All Randomized	All available data will be included Missing data will not be imputed	N/A
Change from baseline at Week 52 in the EQ-5D-5L VAS assessment (caregivers of participants)	Summary	Caregivers of participants in the All Randomized	All available data will be included Missing data will not be imputed	N/A
Change from baseline at Week 52 in the EQ-5D-5L index score (caregivers of participants)	Summary	Caregivers of participants in the All Randomized	All available data will be included Missing data will not be imputed	N/A
Immune response				
ADA to mini-dystrophin	Summary	Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
T cell response to mini-dystrophin by peptide pool	Summary	Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
ADA to AAV9	Summary Box-plots for observed levels	Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
NAb to AAV9	Summary Box-plots for observed levels	Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
T cell response to AAV9 by peptide pool	Summary Box-plots for observed levels	Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
Viral Vector Shedding For each of the matrices: blood, saliva, urine				
Viral vector shedding	Summary	Viral Vector Shedding subset of Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
Peak viral vector shedding	Summary	Viral Vector Shedding subset of Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
Time of peak viral vector shedding	Summary	Viral Vector Shedding subset of Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A

Endpoint	Analysis Type	Population	Data Inclusion and Rules for Handling Intercurrent Events and Missing Data	Analysis Model
Time to undetectable viral vector (time to clearance of viral vector)	Plot of K-M-estimates Summary including median times and ranges of times	Viral Vector Shedding subset of Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A
Time to the last undetectable viral vector	Plot of K-M-estimates Summary including median times and ranges of times	Viral Vector Shedding subset of Safety Analysis Set (through Week 52)	All available data will be included Missing data will not be imputed	N/A

Appendix 2. Data Derivation Details

Appendix 2.1. Definition and Use of Analysis Visit Windows in Reporting

The below analysis windows will be used for the efficacy parameters. If multiple values are observed within a window, the value closest (and prior) to the target day will be included in the analysis. If multiple values are observed within the same day, the worst value will be included in the analysis.

Efficacy Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit[2]
NSAA, actigraphy, ankle range of motion	Week 9	60	50	70
	Week 18	120	100	140
	Week 35	240	200	280
	Week 52	360	300	390
CK levels	Week 1, Day 4	4	2	7
	Week 2, Day 14	14	11	17
	Week 3	21	18	24
	Week 4	28	25	31
	Week 5	34	32	41
	Week 7	48	42	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	140
	Week 35	240	200	280
	Week 52	360	300	390
Muscle biopsy	Week 52	360	300	390
%pFVC, EQ-5D-Y (proxy), EQ-5D-5L (caregivers of participants)	Week 52	360	300	390
PODCI	Week 35	240	200	280
	Week 52	360	300	390

1. Relative to Day 1 (day of IP administration)
2. If Year 2 Day 1 IP is administered after Day 390, the upper limit for the Week 52 window will be Day 390. If Year 2 Day 1 IP is administered on or prior to Day 390, the upper limit for the Week 52 window will be one day before the day of Year 2 Day 1 IP administration.

The below analysis windows will be used for the immunogenicity parameters. If multiple values are observed within a window, the value closest (and prior) to the target day will be included in the analysis.

Immunogenicity Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit[2]
ADA to mini-dystrophin	Week 2, Day 14	14	2	17
	Week 3	21	18	24
	Week 4	28	25	31
	Week 5	34	32	41
	Week 18	120	100	140
	Week 52	360	300	390

ADA to AAV9	Week 5	34	20	48
	Week 18	120	100	140
	Week 52	360	300	390
NAb	Week 5	34	20	48
	Week 52	360	300	390
T cell response	Week 9	60	50	70

1. Relative to Day 1 (day of IP administration)
2. If Year 2 Day 1 IP is administered after Day 390, the upper limit for the Week 52 window will be Day 390. If Year 2 Day 1 IP is administered on or prior to Day 390, the upper limit for the Week 52 window will be one day before the day of Year 2 Day 1 IP administration.

The below analysis windows will be used for the safety parameters. If multiple values are observed within a window, the worst value will be included in the analysis.

Safety Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit[2]
CK levels (higher values are worse)	Week 1, Day 4	4	2	10
	Week 2, Day 14	14	11	17
	Week 3	21	18	24
	Week 4	28	25	31
	Week 5	34	32	41
	Week 7	48	42	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
Creatinine (higher values are worse)	Week 1, Day 2	2	2	3
	Week 1, Day 4	4	4	5
	Week 1, Day 6	6	6	6
	Week 1, Day 7	7	7	7
	Week 2, Day 8	8	8	8
	Week 2, Day 9	9	9	9
	Week 2, Day 10	10	10	12
	Week 2, Day 14	14	13	17
	Week 3	21	18	27
	Week 5	34	28	41
	Week 7	48	42	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
GLDH levels (higher values are worse)	Week 1, Day 2	2	2	3
	Week 1, Day 4	4	4	6
	Week 2, Day 9	9	7	11
	Week 2, Day 14	14	12	17
	Week 3	21	18	24
	Week 4	28	25	31

Safety Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit[2]
	Week 5	34	32	41
	Week 7	48	42	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
Platelets (lower values are worse)	Week 1 Day 2	2	2	3
	Week 1, Day 4	4	4	5
	Week 1, Day 6	6	6	6
	Week 1, Day 7	7	7	7
	Week 2, Day 8	8	8	8
	Week 2, Day 9	9	9	9
	Week 2, Day 10	10	10	12
	Week 2, Day 14	14	13	17
	Week 3	21	18	27
	Week 5	34	28	47
	Week 9	60	48	75
	Week 13	90	76	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
GGT levels (higher values are worse)	Week 1 Day 2	2	2	3
	Week 1, Day 4	4	4	9
	Week 2, Day 14	14	10	17
	Week 3	21	18	27
	Week 5	34	28	41
	Week 7	48	42	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
C3, C4 levels (lower values are worse)	Week 1, Day 2	2	2	3
	Week 1, Day 4	4	4	5
	Week 1, Day 6	6	6	6
	Week 1, Day 7	7	7	7
	Week 2, Day 8	8	8	8
	Week 2, Day 9	9	9	9
	Week 2, Day 10	10	10	12
	Week 2, Day 14	14	13	17
	Week 3	21	18	27
	Week 5	34	28	47
Cardiac Troponin I levels (higher values are worse)	Week 1 Day 2	2	2	3
	Week 1, Day 4	4	4	5
	Week 1, Day 6	6	6	7
	Week 2, Day 8	8	8	9
	Week 2, Day 10	10	10	12
	Week 2, Day 14	14	13	17

Safety Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit[2]
	Week 3	21	18	24
	Week 4	28	25	31
	Week 5	34	32	37
	Week 6	42	38	45
	Week 7	48	46	54
	Week 9	60	55	67
	Week 11	74	68	82
	Week 13	90	83	105
	Week 18	120	106	240
	Week 52	360	241	390
Vital Signs[a]	Week 1 Day 1	1	1	1
	Week 1 Day 2	2	2	3
	Week 1, Day 4	4	4	5
	Week 1, Day 6	6	6	6
	Week 1, Day 7	7	7	7
	Week 2, Day 8	8	8	8
	Week 2, Day 9	9	9	9
	Week 2, Day 10	10	10	12
	Week 2, Day 14	14	13	17
	Week 3	21	18	27
	Week 5	34	28	47
	Week 9	60	48	75
	Week 13	90	76	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
ECGs[b]	Week 1 Day 1	1	1	2
	Week 1, Day 7	7	3	9
	Week 2, Day 14	14	10	17
	Week 3	21	18	27
	Week 5	34	28	47
	Week 9	60	48	75
	Week 13	90	76	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390

a: If multiple values are observed within a window, the average of all those values will be used.
b: For quantitative values, if multiple values are observed within a window, the average of all those values will be used. For qualitative values, if multiple visits are windowed, the abnormality flag will be used in generating the incidence of abnormality.

The below analysis windows will be used for viral vector shedding. If multiple values are observed within a window, the largest value will be included in the analysis.

Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit
Viral vector shedding (Whole blood)	Week 1, Day 2	2	2	2
	Week 1, Day 4	4	3	11
	Week 3	21	12	40
	Week 9	60	41	75

Parameter	Visit label	Target day[1]	Window lower limit	Window upper limit
	Week 13	90	76	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390
Viral vector shedding (urine and saliva)	Week 1, Day 1	1	1	1
	Week 1, Day 2	2	2	2
	Week 1, Day 4	4	3	5
	Week 1, Day 7	7	6	8
	Week 2, Day 10	10	9	11
	Week 2, Day 14	14	12	16
	Week 3	21	17	25
	Week 5	34	26	47
	Week 9	60	48	75
	Week 13	90	76	105
	Week 18	120	106	180
	Week 35	240	181	300
	Week 52	360	301	390

1. Relative to Day 1 (day of IP administration)
2. If Year 2 Day 1 IP is administered after Day 390, the upper limit for the Week 52 window will be Day 390. If Year 2 Day 1 IP is administered on or prior to Day 390, the upper limit for the Week 52 window will be one day before the day of Year 2 Day 1 IP administration.

Appendix 2.2. Endpoint Derivations

Appendix 2.2.1. Modified PODCI (Pediatric Parent):

For this study, a modified PODCI scale is being used where questions supporting only two PODCI subscale scores (ie, Transfer and Basic Mobility Core Scale and the Sports and Physical Functioning Core Scale) are being collected. The Pediatric Parent version will be completed by caregivers of participants.

Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent):

The 11 items from the modified PODCI scale are mapped to the original PODCI scale using the below mapping strategy:

Modified	Original	
Q1	Q7	Put on his/her coat?
Q5	Q21	Climb one flight of stairs?
Q8	Q24	Walk one block?
Q9	Q25	Get on and off a bus?
Q12	Q28	Stand while washing his/her hands and face at a sink?
Q13	Q29	Sit in a regular chair without holding on?
Q14	Q30	Get on and off a toilet or chair?
Q15	Q31	Get in and out of bed?
Q16	Q33	Bend over from a standing position and pick up something off the floor?
Q17	Q34	How often does your child need help from another person for sitting and standing?

Modified	Original	
Q18	Q35	How often does your child use assistive devices (such as braces, crutches, or wheelchair) for sitting and standing?

The below algorithm is then applied to the mapped values to calculate the standardized score.

component	value	Result
Notes:	Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.	
	A minimum of 7 items must have valid answers to score this scale (including those marked "too young" as missing).	
	Q34 is RESCALED as follows: Q34rescaled = [(Q34 - 1)* 3/4] + 1	Value ranging 1 to 4
	Q35 is RESCALED as follows: Q35rescaled = [(Q35 - 1)* 3/4] + 1	Value ranging 1 to 4
Mean of Items:	(sum of items Q7, Q21, Q24, Q25, Q28, Q29, Q30, Q31, Q33, Q34Rescaled, Q35Rescaled) / (number of non-missing items)	Value ranging 1 to 4
Standardized Score:	[(4 - mean of items) / 3] * 100	Value ranging 0 to 100

Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent):

The 21 items from the modified PODCI scale are mapped to the original PODCI scale using the below mapping strategy:

Modified	Original	
Q2	Q18	Run short distances?
Q3	Q19	Bicycle or tricycle?
Q4	Q20	Climb three flights of stairs?
Q6	Q22	Walk more than a mile?
Q7	Q23	Walk three blocks?
Q10	Q26	How often does your child need help from another person for walking and climbing?
Q11	Q27	How often does your child use assistive devices (such as braces, crutches, or wheelchair) for walking and climbing?
Q19	Q36	Can your child participate in recreational outdoor activities with other children the same age?
Q20		Note: conditional on Q42 Too young?
Q21		Note: conditional on Q43 Activity not in season?
Q22	Q44	Can your child participate in pickup games or sports with other children the same age?
Q23		Note: conditional on Q50 Too young?
Q24		Note: conditional on Q51 Activity not in season?
Q25	Q52	Can your child participate in competitive level sports with other children the same age?
Q26		Note: conditional on Q58 Too young?
Q27		Note: conditional on Q59 Activity not in season?

Modified	Original	
Q28	Q60	How often in the last week did your child get together and do things with friends?
Q29		Note: conditional on Q65 Friends not around?
Q30	Q66	How often in the last week did your child participate in gym/recess?
Q31		Note: conditional on Q72 School not in session?
Q32		Note: conditional on Q73 Does not attend school?

The below algorithm is then applied to the mapped values to calculate the standardized score.

component	value	Result
Notes:	Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.	
	A minimum of 6 items must have valid answers to score this scale (including those marked "too young" as missing).	
	Q26 is RESCALED as follows: Q26rescaled = [(Q26 -1) * 3/4] + 1	Value ranging 1 to 4
	Q27 is RESCALED as follows: Q27rescaled = [(Q27 -1) * 3/4] + 1	Value ranging 1 to 4
	Q36 is RECODED to MISSING if (Q36 = 4 and EITHER [Q42 = ”Y”] or [Q43 = ”Y”])	Value ranging 1 to 4
	Q44 is RECODED to MISSING if (Q44 = 4 and EITHER [Q50 = ”Y”] or [Q51 = ”Y”])	Value ranging 1 to 4
	Q52 is RECODED to MISSING if (Q52 = 4 and EITHER [Q58 = ”Y”] or [Q59 = ”Y”])	Value ranging 1 to 4
	Q60 is RECODED and RESCALED as follows:	
	Step #1: Q60 is RECODED to MISSING if (Q60 = 3 and Q65 = ”Y”)	
	Step #2: If Q60 is not missing, Q60rescaled = [(Q60 -1) * 3/2] + 1	Value ranging 1 to 4
	Q66 is RECODED and RESCALED as follows:	
	Step #1: Q66 is RECODED to MISSING if (Q66 = 4)	
	Step #2: Q66 is RECODED to MISSING if (Q66 = 3 and EITHER [Q72 = ”Y”] or [Q73 = ”Y”])	
	Step #3: If Q66 is not missing, Q66rescaled = [(Q66 - 1) * 3/2] + 1	Value ranging 1 to 4
Mean of Items:	(sum of items Q18, Q19, Q20, Q22, Q23, Q26rescaled, Q27rescaled, Q36, Q44, Q52, Q60rescaled, Q66rescaled) / (number of non-missing items)	Value ranging 1 to 4
Standardized Score:	[(4 - mean of items) / 3] * 100	Value ranging 0 to 100

Appendix 2.2.2. Categorical Classes for ECG of Potential Clinical Concern

Categories for QTcF

	Borderline	Prolonged	
QTcF (msec)	450≤ max. <480	480≤ max.<500	max. ≥500

QTcF (msec) increase from baseline	30≤ max. <60	max. ≥60

Categories for PR interval and QRS complex

PR interval (msec)	max. ≥300	
PR interval (msec) increase from baseline	Baseline >200 and max.≥25% increase	Baseline ≤200 and max. ≥50% increase
QRS complex (msec)	max. ≥140	

Note:Additional summary for QRS complex and heart rate may be conducted

Appendix 2.3. Definition of Protocol Deviations That Relate to Statistical Analyses/Populations

Not applicable.

Appendix 3. Data Set Descriptions

None.

Appendix 4. Statistical Methodology Details

None.

Appendix 5. Sample SAS Code

Appendix 5.1. Sample SAS Code for The Primary Analysis with Unstructured Covariance

```
proc mixed data=nsaa_pb;

  class subjid trt01pn visitn;

  where avisit in ("Week 9" "Week 18" "Week 35" "Week 52") & param = 'NSAA Total
Score';

  model  chg = trt01pn base agemodel visitn trt01pn*visitn base*visitn agemodel*visitn/
DDFM=KenwardRoger;

  repeated visitn/ type=un subject=subjid ;

     lsmeans trt01pn*visitn/ diff alpha=0.05 CL ;

     lsmestimate trt01pn*visitn 'LSM Difference at Week 52' 0 0 0 1 0 0 0 -1/alpha=0.05 cl;
```

```
 run;
```

Appendix 5.2. Sample SAS Code for The Primary Analysis with Spatial Power Covariance

```
proc mixed data=nsaa_pb;

   class subjid trt01pn visitn;

   where avisit in ("Week 9" "Week 18" "Week 35" "Week 52") & param = 'NSAA Total
Score';

   model  chg = trt01pn base agemodel visitn trt01pn*visitn base*visitn agemodel*visitn/
DDFM=KenwardRoger;

   repeated visitn/ type= SP(POW)(visitn) subject=subjid ;

       lsmeans trt01pn*visitn/ diff alpha=0.05 CL ;

       lsmestimate trt01pn*visitn 'LSM Difference at Week 52' 0 0 0 1 0 0 0 -1/alpha=0.05 cl;

 run;
```

Appendix 5.3. Sample SAS Code for the Number of Skills Gained at Week 52 Analysis

```
/*save overall baseline mean as variable base_mean*/

proc sql;

    select avg(denomi) into: base_mean

    from adrs2 where ^missing(TRT01P);

Quit;

%put &base_mean;

proc glimmix data=adrs2;

  class  TRT01P;

  model  prop_skills = TRT01P agemodel / dist=bin  link=logit chisq ddfm=NONE;

       lsmeans TRT01P / cl ilink ;

            lsmeans TRT01P / at agemodel=4 cl ilink ;

            lsmeans TRT01P / at agemodel=5 cl ilink ;
```

```
        lsmeans TRT01P / at agemodel=6 cl ilink ;
        lsmeans TRT01P / at agemodel=7 cl ilink ;
        estimate 'Treat diff' TRT01P 1 -1 / cl ilink;
        ods output LSMeans=means4 estimates=est4;
run;

Data means5;
        set means4 ;
        extimate_MU_Gained=(MU)*&base_mean;
       if agemodel ^in (4, 5, 6, 7) & ^missing(TRT01P);
 run;
```

Appendix 6. SAP Amendment History

The summary of changes for the current SAP amendment are described in Section 1. The summary of changes for past amendments can be found below.

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 21-Jul-2019	Original	Not applicable	Not applicable
2 04-Mar-2020	Amendment 1	Updates following regulatory feedback and protocol amendment	SAP split into two documents – one for Primary Analysis through Week 52 and one for Cohort 2 delayed treatment and Long-Term safety and efficacy

			tion 2.1.1 • Estimand 2 no longer to be used for secondary endpoints • Pulmonary function (%pFVC) changed from secondary to tertiary/exploratory endpoint • Clarification of PODCI scales being used • Passive ankle range of motion added as tertiary/exploratory endpoint • Time to loss of ambulation endpoint changed to Loss of ambulation (binary) endpoint • Quality of life EQ-5D-Y (proxy assessment) endpoint clarified • DXA scan endpoints (Bone mineral density and muscle mass) removed • Evaluation of viral vector shedding added as tertiary/exploratory endpoint
			Section 2.1.3 • Background and protocol-mandated glucocorticoid regimens amended • Non-adherence to background or protocol-mandated glucocorticoid regimen amended
			Section 2.2.1 • Sample Size Determination added
			Section 2.2.3 • Siblings – definition and inclusion in analyses added
			Section 3.2 • Details for percent normal mini-dystrophin expression level endpoint added • Endpoint: Change from baseline at Week 52 in %pFVC moved to Section 3.3.1 • Endpoints for PODCI scales clarified

			Section 3.3.1 • Endpoint: Change from Baseline at Week 52 in passive ankle range of motion (dorsiflexion) added • Details on endpoints for Change from baseline at Week 52 in real-life function parameters as assessed by actigraphy were added • Endpoint: Loss of ambulation through Week 52 was defined in place of Time to loss of ambulation • Endpoint: Change from Baseline at Week 52 in %pFVC moved from Section 3.2 • Endpoints for Quality of life EQ-5D-Y proxy assessment were clarified • DXA scan endpoints (Bone mineral density and muscle mass) removed
			Section 3.3.2 • Immune response endpoints clarified
			Section 3.3.3 • Viral vector shedding endpoints added
			Section 3.4.2 • Summary of glucocorticoid use at Screening added • DMD diagnosis details included
			Section 3.5.1 • Analysis of adverse events by 3-tier approach removed • Subgroup of fracture related AEs removed
			Section 3.5.2 • Laboratory parameters to be analyzed clarified
			Section 3.5.3 • Echocardiogram and Child Behavior Checklist endpoints added

			Section 4 • Analysis populations with regards to siblings clarified • Biopsy and viral vector shedding populations defined
			Section 5.1 • The procedure to control the experiment-wise Type 1 error rate for the primary and select secondary endpoints was changed to gatekeeping and fixed sequence procedures from Hochberg procedures, and the number of secondary endpoints to be considered was reduced by removing the two PODCI endpoints • The analysis plans for the two interim analyses (IAs) will be provided in a separate document • Clarified that if any Type 1 error rate is spent at an interim analysis, the final experiment-wise Type I error rate will be adjusted accordingly
			Section 5.2.3 • Analysis of endpoint by Poisson count methods changed to analysis by binomial methods
			Section 5.3 • Method to handle missing data was changed from jump-to-reference to copy increment in reference • Tipping point analysis added
			Section 6.1 • Clarified that the primary objective and hypotheses will be tested using the Week 52 LS Means from the MMRM model • Clarified sensitivity and supplemental analyses and added tipping point analysis
			Section 6.2.3 • Amended analysis approach for number of skills gained and number of skills either improved or maintained • Clarified sensitivity and supplemental analyses and added tipping point analysis

			Section 6.3.1 • Analysis for endpoint passive ankle range of motion (dorsiflexion) was added
			Section 6.3.2 • Analysis for parameters assessed by actigraphy was added
			Section 6.3.3 • Analysis of time to loss of ambulation was amended to be for the endpoint loss of ambulation
			Section 6.3.4 • Analysis for %pFVC was moved
			Section 6.3.6 • Analysis for immune responses was amended to include titer levels
			Section 6.3.7 • Analyses for viral vector shedding endpoints were added
			Section 6.5.1 • Summarization methods for background glucocorticoid regimen were clarified
			Section 6.5.3 • Calculation of actual administered fordadistrogene movaparvovec dose added • Summarization method for study treatment exposure was added
			Section 6.6.1 • Analysis of adverse events (AEs) by 3-tier approach was deleted. • Summary of fracture related AEs removed
			Section 6.6.2 • Analysis of special lab parameters was clarified, including cardiac troponin I • Analysis of potential liver injury by Hy's law was added
			Section 6.6.6 • Analysis of echocardiogram endpoints was clarified

			Section 6.6.7 • Analysis of Child Behavior Checklist was clarified
			Section 7 • Interim analyses content was abbreviated as the analysis plan for the two IAs will be provided in a separate document
3 30-Sep-2020	Amendment 1	Updates following regulatory feedback	tion 5.2.1.4, Section 6.1.1.6 and Appendix 1 • Removed analysis to leverage external control data
		Based on protocol administrative change letters	Section 3.3.1 • Changed 10 meter run/walk to the walk item of the NSAA
			Throughout the SAP • Changed the timing of muscle biopsies from 'Day 60 (or Day 360)' to 'Day 360'
		SAP content clarification	Section 2.1.3 • Clarified the definition of change in background glucocorticoid regimen
			Section 3.2 • Clarified the LC-MS assay
			Section 3.3.2 • Added observed levels for ELISpot to dystrophin and ELISpot to AAV9
			Sections 3.3.3 and 6.3.7 • Changed the unit of viral vector levels to vector genomes/ml • Added the definition of a negative viral vector result
			Section 3.4.2 and 6.5.1 • Removed item #7 Caregiver demographic characteristics
			Section 3.5.3 • Removed 'peak' from 'Myocardial peak circumferential strain -Global: %' • Added definition for administered dose of IP

			Section 5.2.3 • Changed 'universe' link transform to 'inverse' link transform
			Sections 6.1, 6.2.3, 6.2.4, and 6.2.5 • Clarified analysis of endpoints by age
			Section 6.3.6 • Added analyses for ELISpot-positive to dystrophin levels and ELISpot-positive to AAV9 levels
			Section 6.5.3 • Added a summary of the percent of planned volume of IP administered • Moved definition of administered dose of IP to Section 3.5.3
			Section 6.5.5 • Added a summary of non-adherence to protocol-mandated and background glucocorticoid regimens
			Section 6.6.2 • Modified Cardiac Troponin I to cTn-I
			Section 6.6.4 • Added a summary for ECG findings of potential clinical concern
			Section 8 • Added McDonald et al 2013 to the list of references
			Appendix 2 • Added analysis windows for viral vector shedding, C3/C4, creatinine, and platelets • Removed raw and normative scores from the Modified PODCI (Pediatric Parent) scoring algorithm
4 14-Jul-2021	Amendment 5	Based on protocol amendment 5	Section 2.1.3 • Updated the algorithm for determining non-adherence to glucocorticoid regimens to align with the protocol and moved to Appendix 2.2.1
		Based on protocol amendment 5	Section 2.2.1 • Modified the text to align with protocol

		SAP content clarification	Section 2.2.2 • Removed all references to the analyses for the Cohort 2 Delayed Treatment period and the long-term follow-up period as these are described in a separate SAP
		Based on protocol amendment 5	Section 2.2.3 • Modified the text to align with the protocol
		SAP content clarification	Section 3.2 • Add an imputation approach for mini-dystrophin expression levels below the limit of quantification • Clarified the conversion of local laboratory and central laboratory CK values to standard units
		Based on protocol amendment 5	Section 3.3.1 • Updated details on the spirometry testing process per the protocol
		Based on protocol amendment 5	Section 3.3.3 and Section 6.3.7 • Added details on sample collection in Japan • Changed DNase to MNase
		SAP content clarification	Section 3.4.2 Clarified DMD diagnoses of interest
		SAP content clarification	Section 3.5 • Added details on the vital signs baseline definition
		Based on protocol amendment 5	tion 3.5.2 • Updated Table 2 per the protocol • Clarified the conversion of local laboratory and central laboratory values to standard units
		Based on protocol amendment 5	Section 3.5.3 • Added protocol text regarding the collection period for non-serious and serious AEs that are to be recorded on the AE CRF
		SAP content clarification	Section 4 • Modified the Viral Vector Shedding population to require at least 2 post-Baseline measurements within first 7 days after fordadistrogene movaparvovec administration to ensure adequate data is collected to determine peak levels

		Based on protocol amendment 5	Section 5 • Modified description/justification of IAs to align with the protocol
		New analysis	Section 6.4 • Added subset analyses based on Screening age strata
		SAP content clarification	Section 6.6.1 • Added a summary of treatment-related serious TEAEs
		SAP content clarification	Section 6.6.2 • Clarified graphical displays for CK and GLDH
		SAP content clarification	Section 6.6.3 • Clarified how multiple records at a particular timepoint will be handled
		Based on protocol amendment 5	Section 7 • Modified description/justification of IAs to align with protocol
		Based on protocol amendment 5	Section 8 • Added spirometry-related references
		Based on protocol amendment 5	Appendix 2.1 • Revised GLDH, creatinine, platelets, cTn-I, and C3/C4 analysis windows as per Schedule of Activities in the protocol

		Based on protocol amendment 5	Appendix 2.2.1
			• Added new appendix to describe the algorithm for determining non-adherence to glucocorticoid regimens
			  • Split algorithm for protocol amendment 1 and amendment 5
			  • Added a table for converting IV protocol-mandated glucocorticoid dose to oral dose
			  • Added the 1.5 mg/kg/day taper step
			  • Modified the 30- and 90-day criteria for the change to background glucocorticoid regimen

5 15-Oct-2021	Amendment 6	Based on protocol amendment 6	Section 2.1.1, Section 3.3.2, Section 6.3.6, and Appendix 1 • Added caregiver health related QoL objective and endpoints, endpoint definitions, and analysis details
		Based on protocol amendment 6	Section 2.1.2 and Section 3.5.3, and Section 6.6.7 • Added cardiac MRI safety endpoints and analysis details
		Based on protocol amendment 6	Section 2.1.3 • Removed 'in all randomized participants' from the descriptions of Estimand 1 and Estimand 2 to align with the revised analysis sets in Section 4
		Based on protocol amendment 6	Section 2.2, Section 2.2.1, and Section 2.2.3 • Revised the study sample size requirement to 99 participants in the FAS
		SAP content clarification	Section 3.2 • Clarified the unit (meter/second) for 10 meter run/walk velocity
		SAP content clarification	Section 3.3.3, Section 6.3.7, and Appendix 1 • Added details to the endpoint definitions and analyses for the 3 ELISpot peptide pools
		Based on protocol amendment 6	Section 3.5.2 Revised Table 2
		Based on protocol amendment 6	Section 4 • Changed the population "Randomly assigned to investigational product" to "All Randomized" and clarified that siblings and those meeting exclusion criterion 15 will be included. • Revised the description of the FAS, Safety (through Week 52), Biceps Brachii Muscle Biopsies, and Viral Vector Shedding populations
		SAP content clarification	Section 5.2.1.1, Section 5.2.1.2, Section 5.2.1.3, Section 5.2.2, Section 5.2.3, and Section 5.3 • Clarified how participants who do not have a baseline and at least one post-baseline measurement are handled in the analyses.
		SAP content clarification	Section 6.2.3 • Clarified that bar charts are to display Week 52 only

		SAP content clarification	Section 6.2.5 and Appendix 1 • Added shift tables for each of the 5 dimensions of the EQ-5D-Y proxy assessment
		SAP content clarification	Section 6.5.1 Clarified that all baseline summaries will be performed for the All Randomized population.
		SAP content clarification	Section 6.5.2 • Added important protocol deviations
		SAP content consistency	Section 6.6.6 • Removed endpoint definition details since they are already contained in Section 3.5.3
		Based on protocol amendment 6	Appendix 2.1 • Revised analysis visit windows for CK (efficacy and safety), ADA to mini-dystrophin, and cTn-I,
		SAP content clarification	Appendix 2.2.1 • Clarified the definition of a change in dose of protocol-mandated glucocorticoids and added criteria regarding the use of other glucocorticoids not allowed per protocol
		SAP content clarification	Appendix 2.2.3 • Removed the ELISpot response level algorithm since the calculations are now performed by the lab vendor
6 21 April 2022	Amendment 8 04-Mar-2022	SAP content clarification	Section 3.2 Updated mini-dystrophin expression level assay details
		SAP content clarification	Section 3.2/ 3.4.2/ 3.5.2/ 6.5.1 /6.5.2/6.5.4/6.6.1/6.6.2/6.6.3/6.6.4 Removed words 'Pfizer data standards'
		SAP content clarification	Section 3.3.1 Added the compliance definition of actigraphy
		SAP content clarification	Section 3.3.3 Removed the ELISpot overall definition
		SAP content clarification	Section 3.4.2 Removed details on mutation diagnostic
		SAP content clarification	Section 3.4.2 & Section 6.5.1 Added Background glucocorticoid regimen daily dose and duration derivation details
		Based on protocol amendment 8	Section 3.5.2, Section 6.6.2, Appendix 2.1, Appendix 4 Added local cTn-I (or cTn-T) laboratory assessments
		Based on protocol amendment 8	Section 3.5.3 Added O2 saturation to vital sign of interest during hospital stay post-IP administration and updated the echo parameter list
		SAP content clarification	Section 4 Added "Safety Analysis Set through Week 52" wording

		SAP content clarification	Section 6.1.1.2 Updated wording for Sensitivity analysis 1
		SAP content clarification	Section 6.1.1.3 Updated wording for Sensitivity analysis 2
		SAP content clarification	Section 6.2.1 Added LC-MS assay for LEMP supplementary peptide
		SAP content clarification	Section 6.2.1.1 Added baseline detail for LC-MS assay
		SAP content clarification	Section 6.2.1.2 Added mini-dystrophin expression level endpoints
		SAP content clarification	Section 6.3.3 Updated analysis set to FAS
		SAP content clarification	Section 6.3.7 Updated wording for the graphical display.
		SAP content clarification	Section 6.5.1 Updated 'Dystrophin mutation type' to 'DMD genetic results'
		Based on protocol amendment 8 and SAP content clarification	Section 6.6.2 If there is a local and central laboratory collection on the same day, the central laboratory value will be used for analysis Added 99th percentile values for cTn-I and details on the post-baseline assessments. Added cTn-I graphical displays
		SAP content clarification	Section 6.3.7 Added Placebo and edited the text for graphical display to the observed titers for ADA-positive to mini-dystrophin participants, ADA-positive to AAV9 participants, and NAb-positive to AAV9 participants
		SAP content clarification	Appendix 1 Updated wording for sensitivity analysis.
		SAP content clarification	Appendix 2.1 Split the safety and viral vector shedding into two tables. Replaced 'largest' value to 'worst' in the safety parameters and explained the 'worst' for each individual parameter.
		SAP content clarification	Appendix 2.2.1 Updated the adherence definition
		SAP content clarification	Appendix 5 Moved the previous modification history to the appendix and keep only the last modification in Section 1.
7 17 Jan 2023	Amendment 12 30-Sep-2022	Per BDR comments	Sections 2.1.1, 3.2, and 6.2.2 Added percent change from baseline at Week 52 in serum CK concentration
		Based on protocol amendment	Section 2.3 Updated the enrollment screening age criteria
		Based on protocol amendment	Section 2.3.1 Updated sample size calculation details and added efficacy and futility boundaries
		SAP content clarification	Section 2.3.2 Aligned the reporting period definition with the revised analysis visit windows in Appendix 2.1
		Based on protocol amendment	Section 2.3.3 Updated the number of participants with muscle biopsies

		SAP content clarification	Section 3.2 Clarified that immunofluorescent staining will use the mini-dystrophin specific antibody
		SAP content clarification	Section 3.3.4 Removed sentences about samples for participants in Japan Clarified the imputation of viral vector shedding values below the lower limit of quantification
		SAP content clarification	Section 3.4.2 Modified definition of screening age strata to reflect the strata in which participants were randomized
		SAP content addition	Section 3.4.2 Added gender in baseline variables
		SAP content addition	Sections 3.4.2 and 6.5.1 Added age at dosing with IP on Year 1 Day 1
		Based on protocol amendment	Section 3.5.2 and 6.6.2 Updated Table 2 based on protocol amendment Updated definition to indicate that normalization will be applied for select laboratory parameters
		SAP content clarification	Section 3.5.3 Added location of some of echo parameters
		Based on protocol amendment	Sections 2.3.1, 5.1, and 7 Updated IA strategy and provided additional details for the efficacy and futility boundaries
		SAP content clarification	Sections 5.4, 6.1.1.6, and 6.2.5.2 Added meaningful within-patient change threshold analysis
		SAP content clarification	Section 6.1.1.5 Modified the analysis population as FAS (Regardless of adherence to glucocorticoid regimen)
		SAP content clarification	Section 6.2.2 Clarified the back-log transformation LS means
		SAP content addition	Section 6.6.1 Added grid plot for treatment-emergent SAEs.
		SAP content updates	Section 6.6.2 Removed summary of changes from baseline for all laboratory parameters; descriptive statistics will only be provided for select laboratory test parameters Added GGT in the select laboratory parameters to be analyzed. For cTn-I, clarified ULN and added details for handling results from the new assay
		SAP content addition	Sections 6.6.3, 6.6.4, and Appendix 2.2.3 Added categorical analyses for vital signs and ECGs.
		SAP content addition	Appendix 1 Added analyses for percent change from Baseline at Week 52 in serum CK Added box-plots for response to AAV9 Added eCDF for NSAA and PODCI

		SAP content updates	Appendix 2.1 Revised the visit windowing to minimize missing data for participants with visits out of protocol-specified visit windows Added GGT visit windowing
		SAP content clarification	Appendix 2.2.1 Clarified non-adherence to background or protocol-mandated glucocorticoid regimens
		SAP content addition	Appendix 2.2.3 New appendix containing categories for ECGs
8 11 Oct 2023	Amendment 14 07-Jun-2023	The endpoint percentage change from baseline at Week 52 in CK serum concentration will be summarized descriptively	Section 2.1.1/3.2 Removed endpoint percentage change from baseline at Week 52 in CK serum concentration Section / 6.2.2 Removed the analyses and summaries for endpoint "percentage change from baseline at week 52 in CK serum concentration" Added descriptive statistics for "percentage change from baseline at Week 52 in CK serum concentration" Added box plots graphical display for percentage change from baseline at Week 52 in CK serum concentration for fordadistrogene movaparvovec and placebo at each visit Appendix 1 Added summary analysis for percentage change from baseline at week 52 in CK serum concentration
		Per FDA Type D meeting feedback received on 26 June 2023	Section 2.2.1 Clarified the intercurrent events and missing data and described the strategy to handle these events Removed the hypothetical estimand
		Per FDA Type D meeting feedback received on 26 June 2023	Section 2.2.2 Clarified the intercurrent events and missing data and described the strategy to handle these events
		To clarify the definition of age stratum	Section 2.3.3 Deleted words "Stratum 1" and "Stratum 2" Removed text "The randomization list for Stratum 1 will be created with randomization numbers from 1-996 and the randomization list for Stratum 2 will be created with randomization numbers 1001-1996."

		Troponin T analysis is not interpretable since it was only collected when Troponin I was not done. Table 2 update is due to protocol amendment	Section 3.5.2 Added safety laboratory assessment for Russia in Table 2. Updated Table 2 footnote. Removed analysis for Troponin T
		To maintain intra-document consistency	Section 3.5.3 Changed “percent of planned volume of IP administered” to “percent of planned dose administered”.
		Per FDA Type D meeting feedback received on 26 June 2023	Section 4 Removed population definition table for adherence to glucocorticoid regimen and Biceps Brachii Muscle Biopsies
		Per FDA Type D meeting feedback received on 26 June 2023	Sections 5.2.1.1/5.2.1.2/5.2.1.3/5.2.2/5.3, Removed text “Participants who do not have a baseline and at least one post-baseline measurement at or prior to Week 52 will be excluded from the analysis.”
		Per FDA Type D meeting feedback received on 26 June 2023	Sections 2.1.1/2.2.1/6.1.1.1/6.2.1/6.2.2/6.2.3/6.2.4/6.2.5/6.4/Appendix 1 Removed text “regardless of adherence to glucocorticoid regimen” and “regardless of adherence to background and protocol-mandated glucocorticoid regimens”
		To clarify the estimand definition (primary or secondary) as estimand 2 is removed	Sections 2.1.1/2.2.1/2.2.2/5.3/6.1.1.1/6.1.1.2/6.1.1.3/6.1.1.6/6.2.1.1/6.2.1.2/6.2.2/6.2.3.1/6.2.4/6.4 Removed text “Estimand 1” and “Treatment Policy” Replace with “Primary Estimand” or “Secondary Estimand”
		To clarify the type 1 error rate spend during IA analysis	Section 5.1 Clarify the type 1 error rate for secondary endpoints
		To avoid convergence issue for binomial model with the log link function	Section 5.2.3 Replaced log link with logit link for binomial model

		To clarify the objective of meaningful within-patient change threshold	Section 5.4 Clarified the objective of meaningful within-patient change threshold
		Per FDA Type D meeting feedback received on 26 June 2023 indicating challenges with interpreting the hypothetical estimand	Section 6.1.1.4 Removed supplementary analysis #1 (Hypothetical Estimand) Section 6.5.5 Removed section "Non-adherence to Protocol-Mandated and Background Glucocorticoid Regimen" Section Appendix 2.2.1 Removed Appendix 2.2.1 Algorithm to determine non-adherence to background or protocol-mandated glucocorticoid regimens
		To evaluate the impact of the quality issues in the assessment of NSAA at Clinical Site 1024	Section 6.1.1.4 Added sensitivity analysis excluding NSAA assessments performed by evaluator with quality issues Section 6.2.3 Added Section header "6.2.3.1 Main Analysis replacing "Analysis" Section 6.2.3.2 Added supplementary analysis for Number of Skills Gained and Skills Improved or Maintained based on the NSAA Section 6.2.4.1 Added Section header "6.2.4.1 Main Analysis replacing "Analysis" Section 6.2.4.2 Added supplementary analysis for Rise from floor velocity and 10 Meter Run/Walk Test velocity
		To assess the impact of age in the model due to the pauses in dosing	Section 6.1.1.5 Added sensitivity analysis replacing age at screening covariate with age at dosing covariate
		To clarify the definition of age strata at screening	Section 6.4 Clarified that age strata at screening would be based on "Randomization Group" collected in CRF
		To obtain baseline summary for FAS and safety analysis set population	Section 6.5.1 Added baseline summaries for FAS and safety analysis set populations

		To ensure the normalization is applied to appropriate laboratory parameters	Section 6.6.2 Clarified the normalization requirement for the select laboratory parameters
		To obtain summary for time to onset of TEAE/serous TEAE and AEs of interest by interval	Section 6.6.1 Added analysis for time to onset of TEAE data and serious TEAE, and AEs of interest summary by interval Removed grid plots displaying the DMD genetic mutations
		To clarify the analysis for select laboratory parameters	Section 6.6.2 Removed shift table for CK Added shift table for Platelets Updated shift table category for GLDH Removed analysis for Troponin T Updated analysis for Troponin I
		Per FDA Type D meeting feedback received on 26 June 2023	Appendix 1 Added sensitivity analysis for primary efficacy endpoints and supplementary analysis for key secondary efficacy endpoints Changed population for Biceps Brachii Muscle Biopsies to FAS
		Based on protocol amendment	Section Appendix 2.1 Revised the analysis windows for ADA to mini-dystrophin Added analysis window for Troponin I
		To align with protocol	Section Appendix 2.2.2 Updated Categorical classes for ECG parameters
		Provide example codes	Section Appendix 5, 5.1, 5.2, and 5.3 Added sample SAS codes for primary analysis with unstructured covariance and spatial power covariance, and the key secondary efficacy endpoint number of skills gained at Week 52
		To maintain consistency with protocol	All Sections Replaced PF-06939926 with fordadistrogene movaparvovec across SAP Changed all instances of “ELISpot to dystrophin “to “ELISpot to mini-dystrophin” throughout the document.
		To update the upper limit of Week 52 window	All sections Changed the upper limit for the Week 52 window from Day 420 to Day 390 throughout the document

		Updated based on FDA Type D meeting feedback received on 26 June 2023 for subset analyses based on screening age strata, and geographic region. To evaluate subset analysis based on baseline NSAA total score	Section 6.4, Appendix 1 Added subset analyses based on screening age strata, baseline NSAA total score, and geographic region

Appendix 7. List of Abbreviations

Abbreviation	Term
ADA	anti-drug antibodies
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of covariance model
AST	aspartate aminotransferase
BDR	blinded data review
BLA	Biologics license application
CBCL	Child Behavior Check List
CI	confidence interval
CK	creatine kinase
CRF	case report form
cTn-I	cardiac troponin I
cTn-T	cardiac troponin T
DMD	Duchenne muscular dystrophy
eCDF	empirical cumulative distribution function
ECG	electrocardiogram
ELISpot	enzyme-linked immune absorbent spot
EQ-5D-Y	EuroQoL 5-Dimensions for youth
EQ-5D-5L	EuroQol 5 Dimension 5 Level
EQ VAS	the EQ-5D-Y visual analogue scale
FAS	full analysis set
GGT	gamma glutamyl transferase
GLDH	glutamate dehydrogenase
GST	global statistical test
IA	interim analysis
ICH	International Council for Harmonisation
IP	investigational product

Abbreviation	Term
IV	intravenous
K-M	Kaplan-Meier
kg	kilogram
LC-MS	liquid chromatography mass spectrometry
LEMP	LEMPSSLMLEVPTHR
LGE	late gadolinium enhancement
LLN	lower limit of normal
LLoQ	lower limit of quantification
LLQV	LLQVAVEDR
LOA	loss of ambulation
LS	least squares
LV	left ventricle
LVEF	left ventricular ejection fraction
MAA	Marketing authorization application
MAR	missing at random
MedDRA	Medical Dictionary for Regulatory Activities
mg	milligram
MMRM	mixed model repeated measures
MNAR	missing not at random
MNase	micrococcal nuclease
MRI	magnetic resonance imaging
MWPC	meaningful within-patient change
NAb	neutralizing antibodies
NSAA	North Star Ambulatory Assessment
O2	oxygen
PDF	probability density function
%pFVC	percent predicted forced vital capacity
PODCI	Pediatric Outcomes Data Collection Instrument
PT	(MedDRA) Preferred Term
Q1	first quartile
Q3	third quartile
QoL	quality of life
QTcF	QTc corrected using Fridericia's formula
REML	restricted maximum likelihood
RSPL	residual subject-specific pseudo-likelihood
RBC	red blood cell
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation
SOC	system organ class
TEAE	treatment-emergent adverse event
TMA	Thrombotic microangiography
ULN	upper limit of normal

Abbreviation	Term
VAS	visual analog scale
vg	vector genomes
WHO	World Health Organization