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

Investigational Product Number:	fordadistrogene movaparvovec (PF-06939926)
Investigational Product Name:	Not Applicable
United States (US) Investigational New Drug (IND) Number:	017598
European Clinical Trials Database (EudraCT) Number:	2019-002921-31
Protocol Number:	C3391003
Phase:	3
Sponsor Legal Address:	Pfizer Inc. 66 Hudson Boulevard East New York, NY 10001

Short Title: A PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF PF-06939926 IN DMD.

Document History

Document	Version Date
Amendment 15	28 December 2023
Amendment 14	07 June 2023
Amendment 13	06 April 2023
Amendment 12	30 September 2022
Amendment 11	09 September 2022
Amendment 10	10 June 2022
Amendment 9	13 May 2022
Amendment 8	04 March 2022
Amendment 7	04 March 2022
Amendment 6	01 September 2021
Amendment 5	14 April 2021
Amendment 4	28 December 2020
Amendment 3	24 November 2020
Amendment 2	05 October 2020
Amendment 1	18 March 2020
Original protocol	22 May 2019

This amendment incorporates all revisions to date, including amendments made at the request of country health authorities and IRBs/ECs and any protocol administrative change letter(s).

Amendment 15 (28 December 2023)

Overall Rationale for the Amendment:

To specify that PCD may occur when at least 90 randomized participants have received Year 1 IP, which will provide > 95% power, as described in Section 9.2 of the protocol, to address the primary objective of the trial.

To clarify that if a participant/caregiver declines Year 2 IP administration, the participant will remain in the study for follow-up with a modified visit schedule.

Additional incorporation of administrative changes and relevant corrections and clarifications.

Protocol Amendment Summary of Changes Table

Description of Change	Brief Rationale	Section # and Name
Substantial Modification(s)		
Clarified the timing of primary analysis (primary completion date).	A sample size of 90 participants randomized and who received Year 1 IP in the study provides >95% power (assuming a delta of 3 from baseline in the NSAA total score; SD=3.5) to address the primary objective of the trial; this allows for the primary analysis to be conducted when at least 90 treated participants have completed Day 360 (Visit 19).	Sections 4.1. Overall Design. 9.3. Populations for Analysis. 9.5.. Interim Analyses.
Provided instructions that participants who decline Year 1 IP administration will be withdrawn from the study, and that those who decline Year 2 IP administration but remain in the study will not attend Visit 18 (if applicable), Visits 20 to 30.2 or receive protocol-mandated glucocorticoid regimen. Prohibited concomitant medications do not apply to these participants.	To ensure follow-up while avoiding hospitalization, the very frequent safety visits post Year 2 IP administration, and the receipt of high doses of glucocorticoids, given that there is no acutely increased risk of an immune reaction.	Section 7.2.1. Withdrawal of Consent. 1.3.1. Schedule of Activities – Year 1 (Screening to Year 1 Day 360), footnote "f"". Also, in Appendices 10.9. Italy, 10.10. Japan, 10.14. Germany,

Description of Change	Brief Rationale	Section # and Name
		10.15. Russia and 10.16. Israel. Section 1.3.2. Schedule of Activities – Year 2 and Long Term Follow Up, footnotes “bb” and “cc”. Also, in Appendices 10.9. Italy, 10.10. Japan, 10.14. Germany, 10.15. Russia and 10.16. Israel. Section 6.5.1. Permitted therapies. Section 6.5.2. Prohibited Therapies. Section 8.2.10. Post IP Intensified Safety Monitoring (at Year 1 and Year 2).
Non-substantial Modification(s).		
Replaced Estimand 1 (Treatment Policy) with the Primary Estimand for the primary endpoint. Clarified that death or loss of ambulation are identified as potential intercurrent events.	Updated based on US FDA Type D meeting feedback received on 26 June 2023.	Sections 1.1. Synopsis. Section 3.1. Efficacy Objectives,

Description of Change	Brief Rationale	Section # and Name
		Estimands, and Endpoints. Section 9.1.1. Estimands
Replaced Estimand 1 (Treatment Policy) for secondary endpoints with Secondary Estimand(s). Clarified that death or loss of ambulation are identified as potential intercurrent events.	Updated based on US FDA Type D meeting feedback received on 26 June 2023.	Sections 1.1 Synopsis. Section 3.1. Efficacy Objectives, Estimands, and Endpoints. Section 9.1.1. Estimands.
Removed Estimand 2 (Hypothetical) for the primary endpoint.	Updated based on US FDA Type D meeting feedback received on 26 June 2023 indicating challenges with interpretation of the hypothetical Estimand.	Sections 1.1 Synopsis. Section 3.1. Efficacy Objectives, Estimands, and Endpoints. Section 9.1.1. Estimands.
Updated "FAS" to "FAS (through Week 52)" and added definition of Efficacy Analysis Set (long-term)	Clarification that FAS analysis would be through Week 52 (double-blind period). Added definition for "Efficacy Analysis Set (Long-term)", the analysis population to be used for long term efficacy analysis in the study.	Section 9.3. Populations for Analysis.
Clarified the p-value boundary to be used for secondary endpoints that are part of the gatekeeping procedure.	Clarified to preserve study wise Type-I error rate (across primary and secondary endpoints).	Section 1.1. Synopsis. Section 9.1. Estimands and Statistical Hypotheses.

Description of Change	Brief Rationale	Section # and Name
Clarified that instructions for the management of SAEs of elevated troponin or myocarditis are provided in Sections 8.2.7 and 8.2.8.	To ensure that relevant instructions are easily accessed.	Section 9.5.1. Data Monitoring Committee.
Clarified that GLDH is not considered sensitive clinical data.	To clarify that ALT/AST but not GLDH kept blinded from sites and from the sponsor on Day 9 in Year 1 and Year 2.	Section 1.3.1 1.3.1. Schedule of Activities – Year 1 (Screening to Year 1 Day 360), footnote "aa". Section 1.3.2 1.3.2. Schedule of Activities – Year 2 and Long Term Follow Up, footnote "x". Country Appendices: 9 (Italy), 10 (Japan), 14 (Germany), 15 (Russia) and 16 (Israel).
Deleted a statement indicating that the primary analysis would be performed when all enrolled participants complete one year of observation following treatment. Deleted information regarding follow up in the study.	To align with other sections in the protocol. The information deleted from Section 2.1 is not part of the rationale for the study.	Section 1.1. Synopsis. Section 2.1. Study Rationale.
Inserted Section 10.10.8 and clarified that for sites in Japan the	To correct an omission in the country appendix.	Appendix 10 (Japan), Section

Description of Change	Brief Rationale	Section # and Name
local testing of haptoglobin is mandatory but the testing of "Other" analytes prothrombin time activated partial thromboplastin time, CRP, Amylase and Lipase) is optional.		8. Clinical Laboratory Tests. Appendix 2. Clinical Laboratory Tests.
Clarifications and minor updates to the text.	To improve the accuracy of the text.	Updates throughout the protocol
Incorporation of updates made by the PACL (Protocol Administrative Change Letter) for Study C3391003 letter, dated 22 November 2023 to indicate that during periods of significant study delay for operational or administrative causes, participants from sites in Israel will be monitored approximately every 6 months.	To allow continuous monitoring for periods of significant delay in study conduct.	Section 1.3.2 Schedule of Activities – Year 2 and Long Term Follow Up, footnote "a". Section 5.3.2 Year 2 IP Administration Eligibility. Country 16: Israel.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

1. PROTOCOL SUMMARY

1.1. Synopsis

Short Title: A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of PF-06939926 in DMD.

Rationale

The purpose of the study is to demonstrate the safety and efficacy of fordadistrogene movaparvovec (PF-06939926) treatment in participants with DMD to support regulatory review for marketing authorization.

Objectives, Estimands, and Endpoints

The primary objective of the study is to demonstrate superior efficacy of treatment with fordadistrogene movaparvovec as compared to placebo. The table below describes the primary and secondary objectives, estimands, and endpoints. Additional exploratory objectives and endpoints address data collected after the time of the primary analysis including those for participants receiving fordadistrogene movaparvovec in Year 2 (Cohort 2) and those collected in the long-term follow-up.

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.	Primary Estimand: 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; Death or loss of ambulation are identified as potential intercurrent events. 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:**
To quantify the mini-dystrophin expression level in the muscle of participants treated with	Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 using a	Secondary Estimand(s):

Objectives	Endpoints	Estimands
fordadistrogene movaparvovec.	liquid chromatography mass spectrometry (LC-MS) assay.	Population: Boys with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years; Variable: Each secondary endpoint; Death or loss of ambulation are identified as potential intercurrent events. 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 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	Change from Baseline at Week 52 in the rise from floor velocity.	

Objectives	Endpoints	Estimands
movaparvovec as compared to placebo.		
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).	

Overall Design

This is a Phase 3, global, multi-center, randomized, double-blind, placebo-controlled study in ambulatory male participants, 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 approximately 55% of dosed participants are in either of the Screening age strata. Enrollment will be assessed periodically, and if an imbalance is noted, then enrollment of the overrepresented stratum may be paused until a more balanced distribution is achieved. 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). 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.

Number of Participants

A sufficient number of participants will be screened to achieve a total of approximately 99 participants in the FAS across two strata (age <6 years and age ≥6 years) with no more than approximately 55% of dosed participants in either of the Screening age strata.

This sample size 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 – 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.

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomized to a cohort.

Intervention Groups and Duration

In the context of this study, treatment will consist of two single intravenous infusions, one of fordadistrogene movaparvovec and one of placebo. Fordadistrogene movaparvovec will be administered as a dose of 2E14 vg/kg. The term investigational product (IP) is used to refer to either fordadistrogene movaparvovec or placebo. A single intravenous infusion of IP will be delivered over approximately 2 to 4 hours with the timing and sequence as follows:

- Cohort 1 will receive a single dose of fordadistrogene movaparvovec on Day 1 (Visit 3) and a single dose of placebo at Day 390 (Visit 20);

- Cohort 2 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.

All participants will be followed for 5 years after the administration of fordadistrogene movaparvovec such that total time on study will be approximately 5 years for Cohort 1 and 6 years for Cohort 2.

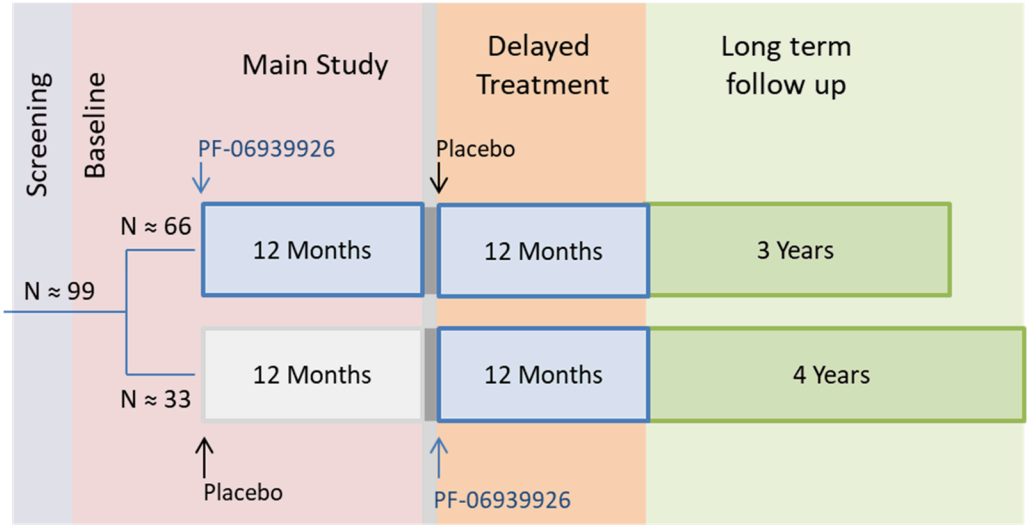
Data Monitoring Committee: Yes

An external data monitoring committee (E-DMC) will be used to provide an ongoing objective, unblinded assessment of safety and efficacy.

Statistical Methods

Primary Estimand: For the primary analysis, change from Baseline at Week 52 in the NSAA total score will be analyzed using a mixed model repeated measures approach including visits through Week 52 where NSAA is assessed. Baseline NSAA total score is defined as the last non-missing NSAA total score collected prior to Year 1 IP administration. The analysis will be based on the Full Analysis Set (FAS) (regardless of adherence to glucocorticoid regimen) and missing data will not be explicitly imputed. The model will include fixed effects for treatment (class variable), visit (class variable), treatment by visit interaction, Baseline NSAA total score (continuous variable), Screening age (continuous variable), Baseline NSAA total score by visit interaction, and Screening age by visit interaction with an unstructured covariance matrix to describe the correlation among different visits from the same participant. Alternative covariance structures to address any issues with model convergence will be specified in the statistical analysis plan (SAP). Estimates at Week 52 of the mean changes from Baseline 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.

1.2. Schema



1.3. Schedule of Activities (SoA)

The SoA table provides an overview of the protocol visits and procedures. Refer to the STUDY ASSESSMENTS AND PROCEDURES section of the protocol for detailed information on each procedure and assessment required for compliance with the protocol.

The investigator may schedule visits (unplanned visits) in addition to those listed in the SoA table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Alternate versions of the SoA for sites in Italy (see Appendix 9), Japan, (see Appendix 10), Germany (see Appendix 14), Russia (see Appendix 15) and Israel (see Appendix 16) are provided.

1.3.1. Schedule of Activities – Year 1 (Screening to Year 1 Day 360)

Period	Screening	Baseline		Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Informed consent/assent	X																						
Inform caregivers about study C3391007[dd]	X																						
Demography	X																						
Medical history	X[ii]																						
Medication history	X																						

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Review of inclusion/exclusion criteria	X	X																					
Eligibility for Year 1 IP administration[v]			X																				
Hospital stay[jj]			X	→	→	→	→	X															
Physical examination[h]	X	X	X	X	X		X		X	X			X			X			X	X		X	X
Neurological examination[h]	X	X			X		X		X	X			X			X			X	X		X	X
Weight		X											X						X	X	X	X	X
Height	X												X						X	X		X	X
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X			X			X	X		X	X
12-Lead ECG[k]	X		X				X			X												X	X
CBCL	X																					X	X[g]
Randomization		X[bb]																					
Laboratory Assessments[l]																							
Blood Samples																							
NAb	X	(X)[cc]											X									X	X[g]

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
ADA to mini-dystrophin and AAV9	X									X[ff]	X[ff]	X[ff]	X						X			X	X[g]
ELISpot to mini-dystrophin and AAV9		X														X							X[g]
Viral Vector Shedding[z]	X			X	X						X					X		X	X	X		X	X[g]
Clinical safety (hematology, other)[l]	X			X	X					X	X		X			X		X	X	X		X	X[g]
Chemistry and hepatic safety[l]	X			X	X					X	X	X[ee]	X		X	X	X	X	X	X		X	X
Post IP intensified safety monitoring[l,w]				X	X					X	X		X										
Local and central laboratory testing[aa]	X[ll]	X		X	X	X	X	X	X	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]		X[ll]	
Cardiac Troponin I	X										X	X	X	X	X	X	X	X	X			X	X

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																					X	
Biomarker (creatine kinase)[l]		X			X					X	X	X	X		X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[m]	X																			X		X	
Banked biospecimens for genetics[n]																		X					
Urine Samples																							
Clinical safety (urinalysis)[l]	X		X	X	X					X			X			X			X			X	X[g]
Banked biospecimens for biomarkers[m]	X																			X		X	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Saliva Samples																							
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Tissue Samples																							
Muscle biopsy[o]		X																				X[x]	
Imaging Assessments																							
Echocardiogram[p]	X																					X	X[g]
Cardiac MRI[gg]	X[hh]																					X[hh]	
Functional Assessments																							
FVC[q,y]	X																					X	X[g]
NSAA[q]	X	X														X			X	X		X	X
Ankle range of motion	X	X														X			X	X		X	X
Ambulatory status	X[r]															X			X	X		X	X
Actigraphy[s]		X														X			X	X		X	
Clinical Outcome Assessments																							
Caregiver-completed																							
Modified PODCI – Pediatric Parent[t]		X																		X		X	X
EQ-5D-Y Proxy[t]		X																				X	X
EQ-5D-5L		X																				X	X
PGIS:CG[t]		X														X			X	X		X	X

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Participant-completed																							
EQ-5D-Y[t]																						X	X
Clinical evaluator-completed																							
CGIS[q]		X														X			X	X		X	X
Health economic questionnaires																							
HRU:CG		X																					
WPAI:DMD Caregiver		X																					
Interventions																							
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X					
Background glucocorticoid regimen	X	X																X	→	→	→	→	
IP administration			X																				
Meningococcal vaccine	X	X																					
Ongoing monitoring																							
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate. Schedule of Activities – Year 2 and Long-Term Follow Up

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;
- Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:
- Schedule A:
    - **First day:** collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place the next day or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.
- Schedule B:
    - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).
- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;
- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);
- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;
- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

b. **Visit 14** and **Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a);
- For sites outside the US, the Baseline visit should occur at least 31 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6)

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);
- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).
- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

l. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings (with the potential to collect a maximum of 33 if needed), at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline Visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline Visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

x. All participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. See Section 8.8.5 for additional details.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 9 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details, please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 4 and 5, see Appendix 2 and Appendix 10 for details.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details- please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. For US sites, only when approved by the relevant Institutional Review Board.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

ee. On Day 28 (Visit 12.2), only GLDH will be collected.

ff. ADA to mini-dystrophin only.

gg. Investigators will discuss with the participant and/or their caregiver the importance of having a baseline cardiac MRI, even under general anesthesia, to be able to assess and manage potential cardiac adverse events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

hh. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

ii. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

jj. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

kk. This visit is for sites in Germany only and only to test cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ll. Only for sites in Russia

1.3.2. Schedule of Activities – Year 2 and Long Term Follow Up

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Eligibility for Year 2 IP administration[r]	X																					
Hospital stay[dd]	X	→	→	→	→	X																
Physical examination[g]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X			X			X	X	X	X	X	X
Height and Weight											X						X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X											X		X	X
CBCL																			X	X	X	X[e]
Laboratory Assessments[k]																						
Blood Samples																						
NAb to AAV9											X								X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X						X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X													X							X[w]	X[e]
Viral Vector Shedding[u]								X						X		X	X	X			X	X[e]
Clinical safety (hematology, other)[k]		X	X					X	X		X			X		X	X	X	X	X	X	X[e]

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Chemistry and hepatic safety[k]		X	X					X	X	X[y]	X		X	X	X	X	X	X	X	X	X	
Post IP intensified safety monitoring[k,s]		X	X					X	X		X											
Local and central laboratory testing[x]	X	X	X	X	X	X	X	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]				
Cardiac Troponin I									X	X	X	X	X	X	X	X	X		X	X	X	X
Biomarker (creatine kinase)[k]			X					X	X	X	X		X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																		X	X			
Urine Samples																						
Clinical safety (urinalysis)[k]	X	X	X					X	X		X			X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																		X	X			
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Saliva Samples																						
Viral Vector Shedding[u]						X				X				X		X	X	X	X		X	X[e]
Tissue Sample																						
Muscle Biopsy																					X[ff]	
Imaging Assessments																						
Echocardiogram[m]																			X		X	X[e]
Cardiac MRI[aa]																			X[aa]			

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Functional Assessments																						
FVC[n,t]																			X		X	X[e]
NSAA[n]														X			X	X	X	X	X	X
Ankle range of motion														X			X	X	X	X	X	X
Ambulatory status														X			X	X	X	X	X	X
Actigraphy[o]														X			X	X	X	X	X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI – Pediatric Parent[p]																		X	X	X	X	X
EQ-5D-Y Proxy[p]																			X		X	X
EQ-5D-5L																			X		X	X
PGIS:CG[p]														X			X	X	X	X	X	X
Participant-completed																						
Modified PODCI – Adolescent[p]																				X	X	X
EQ-5D-Y[p]																			X		X	X
PGIS[p]																				X	X	X
Clinical evaluator-completed																						
CGIS[n]														X			X	X	X	X	X	X
Health economic questionnaires																						
HRU:CG																			X		X	X
WPAI:DMD Caregiver																			X		X	X

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Study Interventions																						
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X						
Background glucocorticoid regimen																X	→	→	→	X[v]	X[v]	
IP administration	X																					
Ongoing monitoring																						
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5 Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. **Visit 20 – Year 2, Week 1, Day 1**

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);
- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed **prior to IP administration**: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.
- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel, see Appendix 16.

b. **Visits 29, 29.2, 30.2, 31.2, and 32**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

c. **Visit 31** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. **Visit 42 and 43 – Long-term follow up Year 6**

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. **Early Discontinuation Visit**

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

f. **Visit Windows for Visits 20 through Visit 43**

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief **physical and neurological examinations,** as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

h. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

j. **12 Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

m. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

n. The **NSAA** and **CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. **An activity monitor** may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

p. **COAs** will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26, 27. For more details please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 21 and 22, see Appendix 2 and Appendix 10 for details.

y. On Day 417 (Visit 29.2), only GLDH will be collected.

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration (see Section 7.2.1) will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12..

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

ee. This visit is for sites in Germany only and only to test cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ff. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

gg. Only for sites in Russia

2. INTRODUCTION

The investigational product (IP), fordadistrogene movaparvovec (PF-06939926), is a gene therapy viral construct (AAV9.hCK.optiDysΔ3978.spolyA), consisting of recombinant adeno-associated virus serotype 9 (AAV9) vector and single stranded deoxyribonucleic acid (DNA) encoding for a miniaturized version of the dystrophin protein ("mini-dystrophin"). The specific coding sequence of the mini-dystrophin gene (OptiDysΔ3978), encompassing domains minimally required for functionality, was chosen based on a published report of a patient and his relatives with a deletion that eliminates 46% of the protein who had a mild disease course consistent with Becker muscular dystrophy (BMD) [England et al., 1990].[1] Cardiac and skeletal muscle specific transgene expression is mediated by the synthetic promoter, hybrid creatine kinase H [Hauser et al., 2000].[2]

Fordadistrogene movaparvovec is intended to be used as a gene replacement therapy, ie, to restore functional dystrophin expression in skeletal and cardiac muscle cells by direct replacement of the missing or dysfunctional protein with mini-dystrophin.

Complete information for this compound may be found in the latest version of the Single Reference Safety Document, which for this study will be the Investigator Brochure (IB).

2.1. Study Rationale

The purpose of the study is to demonstrate the safety and efficacy of fordadistrogene movaparvovec in participants with DMD to support regulatory review for marketing authorization.

2.2. Background

2.2.1. Duchenne Muscular Dystrophy

DMD is a severe, X-linked, progressive neuromuscular disease affecting approximately one in 3600 to 9300 live male births.[3] It is caused by mutations in the dystrophin gene that eliminate or severely reduce the expression of functional dystrophin protein.[4] The near lack of the dystrophin protein in skeletal muscles, including those required for respiration, and in the heart leads to muscle degeneration which results in loss of ambulation and premature death.[5]

First identified in 1987, the dystrophin gene is one of the largest human genes at 2.4 Mb and contains 79 exons.[4,6,7] The most common forms of mutations that cause DMD are large deletion mutations of one or more exons (approximately 68%); however, large duplication mutations (approximately 11%), point mutations (approximately 11%), and small insertion/deletion mutations (approximately 7%) also occur.[8] These gene mutations often lead to a frame shift mutation (ie, disruption of the reading frame) or generate a premature stop codon (ie, out of- frame) and result in absence or significant reduction in the level of functional dystrophin protein. In-frame deletions result in a milder form of muscular dystrophy, ie, Becker muscular dystrophy (BMD), in which patients express a smaller, partially functional dystrophin protein. The deletions in BMD most often involve regions encoding the central rod-like domain, such that the C- and N-terminal domains can still make

the appropriate protein-protein interactions within the cell.[7] There is a wide spectrum of clinical presentations of BMD, ranging from minor effects on lifestyle and lifespan to loss of ambulation in the late teens or early 20s. The most common cause of premature death in BMD patients is cardiac failure.

The clinical course of DMD is a direct result of the rate of damage to the muscle tissue. Skeletal muscles that experience the greatest mechanical stress and have the largest diameter are damaged the fastest (Petrof et al., 1993).[9] At approximately the age of 6, many of the lower extremity muscles begin to lose the ability to regenerate and the degenerative process becomes dominant.[10] As necrosis continues, the loss of muscle is accompanied by an increase in fatty and connective tissue (Ramos et al., 2015),[11] ultimately leading to the loss of ambulation by age 8-11 (Humbertclaude et al., 2012).[12] With continued disease progression, functional loss of the muscles of respiration and the upper extremity can occur.[13] DMD is a terminal disease and patients usually die in the third decade (Kieny P et al, 2013).[14] Eventually, almost all DMD patients develop cardiomyopathy. (Aartsma-Rus et al., 2016)[15] Respiratory and cardiac complications are major causes of disease-related morbidity and mortality.[18]

Standard of care guidelines for DMD multi-disciplinary teams have been developed and were published initially in 2010 and more recently in 2018.[13,16,17,18,19] Current treatment recommendations are aimed at keeping the patient independent for as long as possible and preventing complications that result from weakness, reduced mobility, and cardiac and respiratory complications.

Glucocorticoid therapy (prednisone, prednisolone, and deflazacort) has been used as the standard treatment for several years and is currently recommended to be discussed with caregivers when a patient is between 4 and 8 years of age. [16] Glucocorticoids can slow the rate of muscle deterioration in DMD and help children retain upper limb strength, respiratory function and prolong independent walking by a median of 3 years.[16,20] Although there are clear benefits to patients with DMD, the numerous side effects associated with chronic glucocorticoid use limit treatment (Bushby et al., 2010; Prednisone Summary of Product Characteristics (SmPC) 2018).[13,21]

Currently, 5 drugs targeting dystrophin restoration have been approved. All are designed to interface with the transcription and translation machinery enabling the production of functional dystrophin protein. Translarna™ (ataluren; PTC Therapeutics) is intended to enable stop codon read-through in approximately 10% of DMD patients with erroneous stop signals (“nonsense” mutations”) in the dystrophin gene.[22,23] Translarna received conditional marketing authorization by the European Medicines Agency (EMA) in July 2014; on February 22, 2016, the Food and Drug Administration issued a Refuse to File Letter to PTC, concluding that the application was not substantially complete to allow for substantial review.[24]

EXONDYS 51™ (eteplirsen, Sarepta Therapeutics) is designed to skip over mutations in the region of exon 51,[25] which occurs in approximately 14% of DMD patients.[23] This approach necessarily results in an ‘internally deleted’ protein which is somewhat shorter than the full-

length protein. EXONDYS 51 was granted accelerated approval in September 2016 by the US Food and Drug Administration based on the surrogate endpoint of increased dystrophin protein production.[26] The EMA announced a negative opinion for a conditional marketing authorization for EXONDYS 51 in May 2018 and confirmed its opinion in September 2018 after re-examination.[27] VYONDYS 53™ (golodirsen; Sarepta Therapeutics) and VILTEPSO™ (viltolarsen; Nippon Shinyaku Pharma) are both designed to skip over mutations in the region of exon 53.[28,29] VYONDYS 53 is indicated for the "treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping", which occurs in approximately 8% of DMD patients. VYONDYS 53 was granted accelerated approval in December 2019 by the FDA based on the surrogate endpoint of increased dystrophin protein production. VILTEPSO was granted accelerated approval in August 2020 by the FDA based on an increase in dystrophin protein in skeletal muscle.[30] AMONDYS 45™ (casimersen; Sarepta Therapeutics) is designed to skip over mutations in the region of exon 45, which occurs in approximately 9% of DMD patients;[31] AMONDYS 45 was granted accelerated approval in February 2021 by the FDA based on the surrogate endpoint of increased dystrophin protein production.[32]

In summary, treatment options are limited because glucocorticoids, which can be used by all patients irrespective of underlying mutation, are symptomatic treatments that slow disease progression only to a limited degree and have known safety issues, and the 3 therapies aimed at restoring dystrophin levels are applicable to approximately 30% of the DMD population. Therefore, there remains a significant unmet medical need for a therapy that will target the underlying pathophysiology, significantly alter disease progression, and be efficacious for the entire DMD population, irrespective of mutation type.

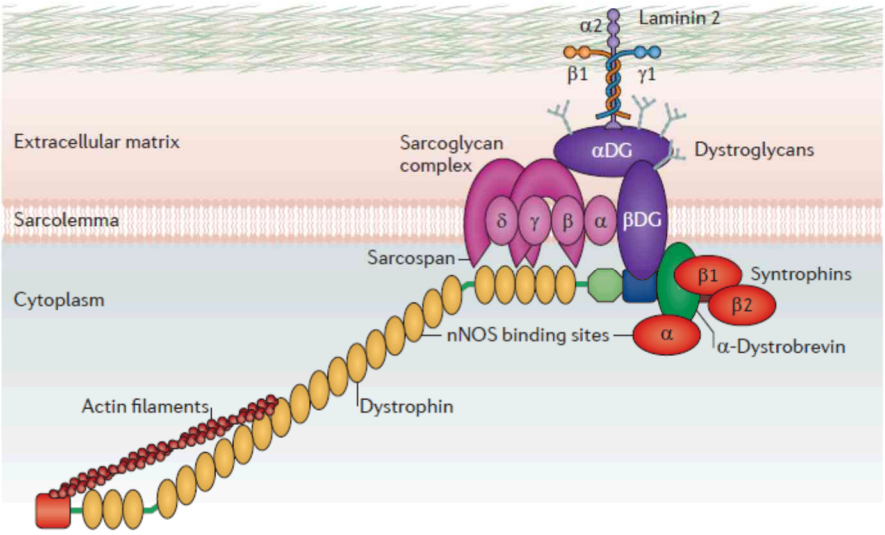
2.2.2. Dystrophin Role in Muscle

In muscle, dystrophin is localized at the cytoplasmic face of the sarcolemma membrane. Full-length dystrophin consists of an N-terminal actin-binding domain, a central large rod-like domain composed of spectrin-like repeats, and a cysteine-rich C-terminus that is connected to the dystrophin-associated glycoprotein complex (DGC), a large protein complex that forms a critical link between the cytoskeleton and the extracellular matrix.[5] The primary function of dystrophin is to act as a shock absorber during muscle fiber contraction, protecting the cell membrane from damage induced by the sheer force.[15]

When dystrophin is significantly reduced, the lack of protection from the stress of contraction leads to sarcolemmal damage, calcium influx, inflammation, and ultimately muscle cell death (ref). This same pathophysiological process occurs in all muscles, although the rate of damage depends on the degree of mechanical stress experienced and the size of the muscle (Petrof et al., 1993).[9] Thus, muscles of the lower limb are affected first, followed by those of the upper limb and those required for respiration.

Figure 1. The Dystrophin-associated Glycoprotein Complex (DGC)

Dystrophin acts as an important link between the internal cytoskeleton and the extracellular matrix. α-dystroglycan (αDG); β-dystroglycan (βDG) [Fairclough et al., 2013].[33]



Due to its pivotal role in the structure of muscle cells, dystrophin restoration, or replacement via gene transfer, requires generation of a form of the protein able to reassemble the DGC and support a mechanically strong link between the extra-cellular matrix and the cytoskeleton [Ehmsen et al., 2002].[34] Based on examples of patients with BMD, the protein can retain this function even when a significant portion of its central rod-like domain is absent.

2.2.3. Gene Therapy for the Treatment of DMD

DMD is an attractive candidate for gene transfer as it arises from mutations in a single gene. Many current gene therapy approaches utilize recombinant AAV (rAAV) vectors to deliver the transgene. rAAV vectors are based on a non-pathogenic, non-integrative, replication deficient member of the parvovirus family and are ideal candidates for muscle-directed gene therapy because of (i) their ability to target skeletal and cardiac muscle, (ii) the long-term persistence of the vector genome in transduced cells, and (iii) their lack of immunotoxicity. [Wang et al., 2000][35] Gene delivery using a variety of AAV serotypes has been investigated in clinical studies for diseases including hemophilia B, alpha-1 antitrypsin deficiency, lipoprotein lipase deficiency, Pompe disease, heart failure, and several muscular dystrophies, including DMD (www.clinicaltrials.gov). Use in this broad spectrum of disease areas is enabling a cumulative experience with the use of rAAV to deliver gene therapy, particularly with regard to safety. The AAV serotype 9 capsid has been shown to have particularly strong and efficient tropism for both skeletal and cardiac muscle, resulting in transduction throughout the body after systemic administration in several preclinical studies [Athanasopoulos et al., 2004; Zincarelli et al., 2008; Wang et al., 2009; Kornegay et al., 2010].[36,37,38,39]

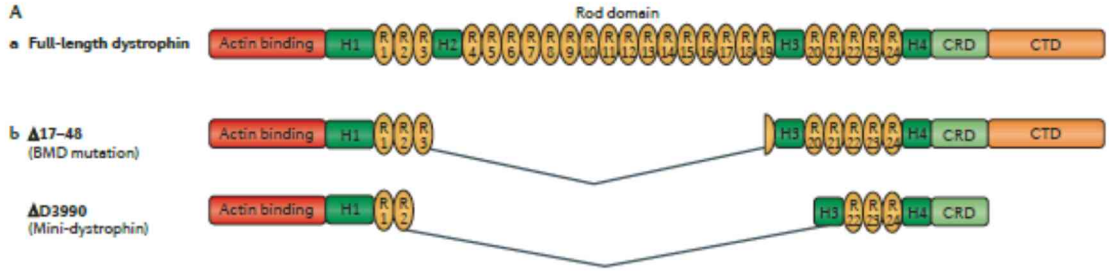
Effective dystrophin restoration or replacement via gene therapy in muscle and cardiomyocytes requires generation of a dystrophin protein able to reassemble the DGC and support a structural link between the extracellular matrix and the cytoskeleton.[11]

A major hurdle in the use of recombinant AAV vectors in dystrophin gene therapy is their packaging capacity, which is approximately 4.7 kb, while the size of the full-length dystrophin complementary deoxyribonucleic acid is about 14 kb. To overcome this challenge, genes with partial deletions of the central rod-like domain that can be successfully packaged inside recombinant AAV vectors have been developed and have been shown in animal models to be functional (Figure 2).[33,40] The mini-dystrophin sequence used in fordadistrogene movaparvovec was designed based on the mutant form of the gene carried in a family of mildly affected patients with BMD in which ambulation was preserved until beyond age 50 (England et al., 1990)[1] Thus, the therapeutic effect of fordadistrogene movaparvovec is anticipated to restore dystrophin function adequate to convert a DMD clinical course into a mild BMD course.

The fordadistrogene movaparvovec sequence has a large in-frame rod domain deletion and fits into AAV vectors even when muscle-specific promoters are incorporated.[33,41] A depiction of the changes, relative to full-length dystrophin, in the family's naturally occurring BMD mutation and in a representative mini-dystrophin gene construct is provided in Figure 2. The mini-dystrophin gene in fordadistrogene movaparvovec has a slightly shorter length but has the same functional domains as the BMD family's mini-dystrophin protein (England et al., 1990).[1]

Figure 2. Schematic of the Domain Components in Full-Length Dystrophin, a Mini-Dystrophin Identified in a BMD Patient and a Mini-Dystrophin tested in DMD Patients

Adapted from Fairclough, et al. 2013.[33]



In animal models of DMD, the mini- or micro-dystrophins, contained within the recombinant AAV vectors have been shown to improve, though not completely normalize, the dystrophic phenotype.[2,33,42,43] Restoration of the dystrophin-associated protein complex, stabilization of muscle degeneration, and improvements in muscle function have been demonstrated following delivery of truncated dystrophin genes at different stages of disease progression in the murine model for DMD.[2,44,45,46] Across several different mini-dystrophin constructs, it has been noted that the ability of the expressed dystrophin proteins to protect muscle from

contraction-induced injury corresponds to both the structural elements included and to the expression levels of the therapeutic protein.[43]

2.2.4. Nonclinical Pharmacodynamics

A dose-finding study of fordadistrogene movaparvovec was conducted in DMD rats and demonstrated a dose-dependent increase in the mini-dystrophin protein expression levels and the percentage of fibers expressing mini-dystrophin, as well as a decrease in fibrosis. [Study PF-06939926_17Aug18_043355 -Mass Spectrometry (IA-LC-MS-MS) quantification of mini-dystrophin protein expression in rat efficacy study]. Additionally, increasing doses of fordadistrogene movaparvovec resulted in a dose-dependent decrease in muscle fatigue as measured by repeat grip testing in the DMD rats. The data from this dose-finding study in DMD rats suggested that 1E14 vg/kg is the minimally effective dose. Specifically, a dose of 1E14 vg/kg resulted in expression of mini-dystrophin in skeletal muscle fibers and cardiac myofibers and was associated with normalization in absolute force and fatigability, as well as improvements in tissue architecture (connective tissue area and overall lesion score) and serum biomarkers. Additionally, expression of the transgene in muscle tissues and preservation of the functional responses persisted 6 months post-dose.

A dose of 3E14 vg/kg was associated with increased transduction and dystrophin expression in muscles relative to that seen for 1E14 vg/kg.

In a biodistribution study with fordadistrogene movaparvovec in the Golden Retriever model of Duchenne dog model, widespread but heterogenous tissue expression levels of the human mini-dystrophin transgene and protein was shown in a subset of the cohort. Histopathological assessments confirmed increased mini-dystrophin positive fibers in the skeletal muscles examined, including the diaphragm. In Golden Retriever model of Duchenne dog studies of mini-dystrophin candidates previously in development, widespread transduction of skeletal muscles and the heart, improvements in the histopathology of muscle tissue and improvement in several measures of function and extended survival were observed.

2.2.5. Nonclinical Immunogenicity

During the evaluation of systemic delivery of fordadistrogene movaparvovec at various doses in the DMD rat model, human mini-dystrophin was recognized by the host immune system; however, the humoral response detected against mini-dystrophin and the AAV9 capsid had no impact on the therapeutic efficacy of the fordadistrogene movaparvovec at 3 and 6 months post-infusion. Consistent with unpublished observations even when the systemic delivery of an AAV encoding for a foreign polypeptide elicits a detectable cellular immune response, it does not necessarily lead to destruction of the transduced cells. The route of administration is believed to be an important component of immune response outcome, with the intravenous (IV) route being the least immunogenic, at least in animal models, including rodents, dogs and nonhuman primates.

2.2.6. Clinical Overview

The ongoing Phase 1b Study C3391001 is the first study of fordadistrogene movaparvovec in humans. It is an open-label, single ascending dose study designed to evaluate the safety and tolerability of the mini-dystrophin gene therapy in ambulatory participants with DMD. The study includes boys with a genetic diagnosis of DMD, age 4 to 12 years, inclusive, who are on a stable dose of glucocorticoids, can rise from the floor in <7 seconds, and are negative for neutralizing antibodies (NAb) to AAV9.

As of 08 January 2020, 3 participants have been treated with the low dose (1E14 vg/kg) and 6 participants have been treated with the high dose (3E14 vg/kg) of fordadistrogene movaparvovec. Muscle biopsies taken from the biceps brachii muscle at 2 months demonstrated robust mini-dystrophin expression. Fordadistrogene movaparvovec was safe and well-tolerated at the low dose, with the most common AEs (in 2 of 3 participants) being transient nausea (1 mild, 1 moderate) and moderate vomiting treated with an oral antiemetic (ondansetron); both events starting at approximately Day 2-5 following treatment. At the high dose, 5 of 6 participants experienced moderate vomiting and 3 of 6 participants experienced moderate nausea and headache (2 mild, 1 moderate), with one participant being re-admitted to the hospital on Day 5 post IP infusion for hydration and IV ondansetron, and thus qualifying as a serious adverse event (SAE). Two additional SAEs (in 2 different participants at high dose) reflected a clinical picture compatible with complement-mediated thrombotic microangiopathy consistent with atypical hemolytic uremic syndrome (aHUS) within two weeks post IP infusion, manifesting with thrombocytopenia, hemolysis, and reversible nephropathy. Medical management, including treatment with eculizumab was provided and led to recovering laboratory test results within 2-3 weeks.

Following the most recent SAE involving complement activation, the Pfizer Benefit-Risk Committee, Pfizer Risk Management Committee, and assigned External Data Monitoring Committee (E-DMC) reviewed the two reported SAEs and full safety information, as well as preliminary evidence of mini-dystrophin expression from muscle biopsies and available data on the NSAA. The outcome of each of these reviews was that the existing safety monitoring remains adequate for mitigating risk and managing these events, and thus, supported the continuation of the trial at the current dose-level.

Study C3391001 will continue to enroll and treat additional participants prior to the start of Study C3391003. Thus, the additional information gained from observing the accruing safety data, from managing the clinical signs and symptoms of any AEs, and from assessing functional outcomes may be used to amend Study C3391003, as needed.

2.2.7. Clinical Pharmacodynamics

As of 20 May 2019, in both the low and high dose cohorts of Study C3391001, muscle biopsies obtained at 2 months post-treatment were evaluated for mini-dystrophin expression and percent of positive fibers. The preliminary results provide some initial evidence of transduction.

2.3. Benefit/Risk Assessment

Given the high unmet medical need for this progressive, fatal, genetic disorder, the potential benefit from gene therapy currently outweighs the known or potential risks.

More detailed information about the known and expected benefits and risks, and reasonably expected adverse events (AEs) of fordadistrogene movaparvovec may be found in the latest version of the Investigator's Brochure (IB) which is the single reference safety document (SRSD) for this study.

An external data monitoring committee (E-DMC) will be used to provide an ongoing objective, unblinded assessment of safety and efficacy (Section 9.5.1). Regulatory authorities will be kept informed of any additional data (eg, results from non-clinical and clinical studies) which may affect the benefit:risk profile for fordadistrogene movaparvovec.

There are three areas of potential risk that are highlighted here, based either on observations from the non-clinical studies, from Study C3391001, or on potential immune reactions to gene therapy.

2.3.1. Delay in Development

In the 90-day toxicology study in juvenile rats, the no observed adverse effect level (NOAEL) was determined to be 3E14 vg/kg because several findings occurred at the next higher dose of 2E15 vg/kg. These findings included decreased body weight and food consumption and delayed skeletal and sexual maturation. Similar findings were not observed in any other non-clinical studies of fordadistrogene movaparvovec. Given the age range of the population included in Study C3391003, in which participants have not completed maturation of the sexual, skeletal, or muscle systems, there is a risk that development of these systems could be affected by therapy, although it is noted that these occurred in the rat study at nearly 10 times the clinical dose. It will be difficult to ascertain the effect of fordadistrogene movaparvovec on development of these systems in Study C3391003 since all participants are required to use daily glucocorticoids, which are also known to cause a delay in skeletal and sexual maturation [Prednisone SmPC].[47]

2.3.2. Immunogenicity Risk Assessment

Humoral and cellular immune responses against both the vector and the transgene may negatively impact the safety and efficacy of gene therapy and will be carefully monitored [Mingozzi et al., 2011].[48] NAb to the vector could significantly reduce muscle cell transduction, and therefore participants with pre-existing NAb are excluded from the study. An immune response to the vector and/or the transgene following treatment can lead to inflammation of tissues that are transduced, such as liver, muscle, and heart, and/or to a systemic immune reaction, such as complement activation, that may result in damage to blood, renal, and possibly other systems.

In order to reduce the possibility of an immune reaction, participants will receive a single IV administration of methylprednisolone prior to the infusion of IP, followed by a protocol-mandated regimen of daily oral glucocorticoids for 3 months, as described in Section 6.5.1.

In a number of on-going or completed clinical studies with AAV-based vectors, the most consistent treatment-emergent adverse reaction reported has been elevations in liver enzymes. Most reported events have resolved with the administration of glucocorticoids (Nathwani).[49] To reduce the risk of liver injury associated with fordadistrogene movaparvovec, participants will receive a single IV administration of methylprednisolone prior to the infusion of IP, followed by a protocol-mandated regimen of oral glucocorticoids for 3 months. Liver injury will be monitored closely using laboratory assessments, including serum glutamate dehydrogenase (GLDH), which is a liver-specific enzyme and is not increased in the setting of muscle disease as is the case for AST and ALT (See Appendix 6).

Cases of skeletal muscle and cardiac injury have been observed in clinical studies of fordadistrogene movaparvovec. The potential for skeletal muscle injury is monitored primarily by physical signs and symptoms, and by measurements of CK, that are monitored on an ongoing basis by the unblinded medical monitor (see Section 6.3.3). The potential for cardiac injury is monitored using cardiac troponin I (see Section 8.2.7). Participants (and/or caregivers) should be instructed to contact the site if signs and symptoms of skeletal muscle and/or cardiac injury are observed (see Section 8.2.11).

Given the SAEs in the Phase 1b Study C3391001, in which subjects had a clinical picture of complement-mediated thrombotic microangiopathy consistent with atypical hemolytic uremic syndrome (aHUS) including thrombocytopenia, indicators of hemolysis, increased serum creatinine from baseline, or low C3 or C4, several risk mitigations have been included in Study C3391003 (see Section 8.2.10).

2.3.3. Risks Related to the Study Design

2.3.3.1. Daily Glucocorticoid Regimen

All participants of this study will be on a background stable daily dose of glucocorticoids for at least 3 months prior to Screening (Visit 1) and will remain on this regimen for at least the first 2 years of the study. Treatment with glucocorticoids to help control the symptoms of DMD and to slow disease progression is a standard therapeutic approach in clinical practice and has been shown to have a positive benefit:risk ratio [https://www.niams.nih.gov/newsroom/spotlight-on-research/optimizing-steroid-treatment-duchenne-muscular-dystrophy]. Given the cumulative side effects of these drugs, however, some physicians choose to wait until a patient begins declining in function to initiate them. There is a potential risk that initiating daily glucocorticoids in boys beginning at 4 years of age could have a long-term impact on their health and/or on the ability to use these medications later in life. This risk is mitigated in this study by allowing participants and their physicians to choose a regimen that they feel best suits the individual participant following completion of Year 2. On rare occasions, participants may develop adrenal insufficiency during the tapering of the protocol-mandated glucocorticoid treatment. Signs and symptoms

of adrenal insufficiency may include hypoglycemia, hyperkalemia, hyponatremia, orthostatic hypotension, hypotension, fatigue, weakness, myalgia, arthralgia, anorexia, abdominal pain, nausea, vomiting and/or diarrhea. Participants with signs or symptoms suggestive of adrenal insufficiency should be promptly evaluated and, if necessary, treated following local guidelines.

2.3.3.2. Muscle Biopsy

To reduce the burden to participants, open muscle biopsies are only being conducted in the minimum number of participants required. This procedure will be performed in Year 1, only on approximately 15 study participants (with the potential to collect a maximum of 33 if needed) randomized into Cohorts 1 and 2 from sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies. The open muscle biopsies will be taken only at Baseline (Visit 2) and twice post-Baseline, on Day 360 (Visit 19) and on Day 1830 (Visit 41), to assess the distribution and amount of mini-dystrophin expression. As with any surgical procedure, complications can occur. These may include bruising, discomfort, bleeding, infection, and/or scarring at the biopsy site. The procedure may be performed under general anesthesia, which has unique risks in the setting of DMD. Although these risks are rare, it is expected that an anesthesiologist with experience treating patients with DMD is involved.

2.3.3.3. Immunity to AAV9

Following administration of fordadistrogene movaparvovec, immunity to AAV9 will be induced. As a result, it will not be possible for a participant treated with fordadistrogene movaparvovec to receive an additional dose of fordadistrogene movaparvovec or any other therapy that utilizes AAV9. Antibodies to AAV9 might also react to other serotypes of AAV and thus prevent treatment with therapies using these other vectors. At this time, there is no known means to mitigate this risk.

2.3.3.4. Participation in Future Clinical Studies

Given the likelihood that the mini-dystrophin gene will persist within cardiac and skeletal muscle for many years (ie, no known wash-out period), it is possible that a participant in Study C3391003 may not be eligible for future studies of other therapies.

2.3.3.5. Human Albumin

Human albumin, at a final concentration of 1.25%, will be used to prepare the IP solution. Risks associated with the use of human albumin include 1) hypersensitivity reactions that may progress to anaphylactic reactions and 2) the transmission of infectious diseases, such as viruses and theoretically, the Creutzfeldt-Jakob disease agent. For more information, please see prescribing information.[50]

2.3.3.6. Sorbitol

Each intravenous infusion of fordadistrogene movaparvovec (and infusion of placebo) contains 5% sorbitol, which is equivalent to 5 mg/mL or 150 mg/kg. Sorbitol is metabolized

into fructose, and products containing sorbitol given intravenously may have life-threatening effects in individuals with hereditary fructose intolerance (HFI) and should not be administered in this population. Although HFI is typically diagnosed in infancy, there can be children or adults with HFI who remain undiagnosed due to dietary management of symptoms. Symptoms suggestive of HFI include nausea, vomiting, bloating, stomach cramps, or diarrhea following the ingestion of foods or drinks containing fructose, or a pattern of avoiding sweet foods or drinks.

2.3.3.7. Gadolinium

A known adverse health effect related to gadolinium retention is a rare condition called nephrogenic systemic fibrosis that can occur in a small subgroup of patients with pre-existing renal failure. Sites will be responsible for confirming participant eligibility to undergo cardiac MRI scanning and gadolinium contrast administration.

3. OBJECTIVES, ESTIMANDS, AND ENDPOINTS

3.1. 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.	Primary Estimand: 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; Death or loss of ambulation are identified as potential intercurrent events. 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:**
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 using an LCMS assay.	Secondary Estimands: Population: Boys with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years; Variable: 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 as assessed by immunofluorescence.	

Objectives	Endpoints	Estimands
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.	Death or loss of ambulation are identified as potential intercurrent events. Population-level summary: difference in means between fordadistrogene movaparvovec and placebo for each secondary endpoint.
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).	
Tertiary/Exploratory:	**Tertiary/Exploratory:**	
To assess the systemic immune response (humoral and cellular) to mini-dystrophin in participants treated with fordadistrogene movaparvovec.	Immune response (eg, anti-drug antibodies (ADA) 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 (eg, 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

Objectives	Endpoints	Estimands
To tabulate loss of ambulation in participants treated with fordadistrogene movaparvovec as 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
To evaluate the efficacy of treatment with fordadistrogene movaparvovec in participants in Cohort 2 after receiving fordadistrogene movaparvovec, based on change in the NSAA.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in the NSAA total score.	N/A
To characterize the change in serum CK concentration in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in serum CK concentration.	N/A
To characterize the skills gained, based on the individual items of the NSAA, in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Number of skills gained from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 based on the individual items of the NSAA.	N/A
To characterize the skills either improved or maintained, based on the individual items of the NSAA, in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Number of skills either improved or maintained from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 based on the individual items of the NSAA.	N/A
To characterize the 10-meter run/walk velocity in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in the 10 meter run/walk velocity.	N/A
To characterize the rise from floor velocity in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in the rise from floor velocity.	N/A

Objectives	Endpoints	Estimands
To characterize the functional health status in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent).	N/A
	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent).	N/A
To assess the systemic immune response (humoral and cellular) to mini-dystrophin and to AAV9 in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Immune response (eg, ADA to mini-dystrophin and ELISpot to mini-dystrophin) after Year 2 Day 1 IP administration through Year 2 Week 52.	N/A
To assess the systemic immune response (humoral and cellular) to mini-dystrophin and to AAV9 in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Immune response (eg, ADA, ELISpot, and NAb) to AAV9 through Year 2 Week 52.	N/A
To characterize the change in ankle range of motion in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in passive ankle range of motion (dorsiflexion).	N/A
To characterize real-life function in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in real-life function parameters as assessed by actigraphy.	N/A
To tabulate loss of ambulation in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Loss of ambulation from pre-fordadistrogene movaparvovec baseline through Year 2 Week 52.	N/A
To characterize pulmonary function in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 in %pFVC.	N/A
To characterize health-related quality of life in participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Response to each of the 5 dimensions of the EQ-5D-Y proxy assessment at Year 2 Week 52.	N/A
	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 on the EQ visual analog scale (VAS) proxy assessment.	N/A
To characterize caregiver health-related QoL in caregivers of participants in Cohort 2 after receiving fordadistrogene movaparvovec.	Response to each of the 5 dimensions of the EQ-5D-5L assessment at Year 2 Week 52.	N/A
	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 on the EQ-5D-5L VAS assessment.	N/A
	Change from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 on the EQ-5D-5L index score.	N/A

Objectives	Endpoints	Estimands
To characterize the long-term efficacy of treatment with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the NSAA total score.	N/A
To quantify the long-term 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 1830 (ie, 4 or 5 years post fordadistrogene movaparvovec administration) using an LC-MS assay.	N/A
To characterize the long-term 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 1830 (ie, 4 or 5 years post fordadistrogene movaparvovec administration) as assessed by immunofluorescence.	N/A
To characterize the long-term skills gained, based on the individual items of the NSAA, in participants treated with fordadistrogene movaparvovec.	Number of skills gained from pre-fordadistrogene movaparvovec baseline to 1, 2, 3, 4, and 5 years post fordadistrogene movaparvovec administration based on the individual items of the NSAA.	N/A
To characterize the long-term skills either improved or maintained, based on the individual items of the NSAA, in participants treated with fordadistrogene movaparvovec.	Number of skills either improved or maintained from pre-fordadistrogene movaparvovec baseline to 1, 2, 3, 4, and 5 years post fordadistrogene movaparvovec administration based on the individual items of the NSAA.	N/A
To characterize the long-term 10-meter run/walk velocity in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the 10 meter run/walk velocity.	N/A
To characterize the long-term rise from floor velocity in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the rise from floor velocity.	N/A
To characterize the long-term functional health status in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the Modified PODCI: Transfer and Basic Mobility Core Scale (Pediatric Parent).	N/A
	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the Modified PODCI: Sports and Physical Functioning Core Scale (Pediatric Parent).	N/A
	Observed scores post fordadistrogene movaparvovec administration in the	N/A

Objectives	Endpoints	Estimands
	Modified PODCI: Transfer and Basic Mobility Core Scale (Adolescent).	
	Observed scores post fordadistrogene movaparvovec administration in the Modified PODCI: Sports and Physical Functioning Core Scale (Adolescent).	N/A
To characterize the long-term systemic immune response (humoral and cellular) to mini-dystrophin and to AAV9 in participants treated with fordadistrogene movaparvovec.	Immune response (eg, ADA to mini-dystrophin and ELISpot to mini-dystrophin) at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration.	N/A
To characterize the long-term systemic immune response (humoral and cellular) to mini-dystrophin and to AAV9 in participants treated with fordadistrogene movaparvovec.	Immune response (eg, ADA, ELISpot, and NAb) to AAV9 at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration.	N/A
To characterize long-term range of motion in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in passive ankle range of motion (dorsiflexion).	N/A
To characterize long-term real-life function in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in real-life function as assessed by actigraphy.	N/A
To characterize time to loss of ambulation in participants treated with fordadistrogene movaparvovec.	Time in years to loss of ambulation.	N/A
To characterize long-term respiratory function in participants treated with fordadistrogene movaparvovec.	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in %pFVC.	N/A
	Peak FVC post fordadistrogene movaparvovec administration.	N/A
To characterize the long-term health-related quality of life in participants treated with fordadistrogene movaparvovec.	Response to each of the 5 dimensions post fordadistrogene movaparvovec in the EQ-5D-Y (proxy).	N/A
	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the EQ VAS (proxy).	N/A
	Response to each of the 5 dimensions post fordadistrogene movaparvovec administration in the EQ-5D-Y (self-report).	N/A
	Observed EQ VAS post fordadistrogene movaparvovec administration (self-report).	N/A

Objectives	Endpoints	Estimands
To characterize the long-term caregiver health-related quality of life 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 pre-fordadistrogene movaparvovec baseline and at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec.	N/A
	Change from pre-fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration in the EQ-5D-5L VAS.	N/A
	Change from pre-fordadistrogene movaparvovec baseline at all timepoints after fordadistrogene movaparvovec administration in the EQ-5D-5L index score.	N/A
To characterize the long-term health resource utilization in participants treated with fordadistrogene movaparvovec.	Health Resource Utilization (HRU:CG) survey responses at Baseline and at Years 1, 2, 3, 4, and 5 post fordadistrogene movaparvovec administration.	N/A
To characterize the long-term caregiver lost work productivity and activity impairment for caregivers of participants treated with fordadistrogene movaparvovec.	WPAI:DMD Caregiver responses (including absenteeism, presenteeism, work productivity loss, and activity impairment) at Baseline and at Years 2, 3, 4, and 5 post fordadistrogene movaparvovec administration.	N/A
To enable exploratory research through collection of banked biospecimens, unless prohibited by local regulations or ethics committee decision.	Potential results from exploratory analysis of banked biospecimens (these results may or may not be generated in the context of the present study).	N/A

3.2. 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) (AEs and 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; • Weight; • Vital signs; • ECG; • Echocardiogram; • Cardiac MRI • Child Behavior Check List (CBCL).

Objectives	Endpoints
To characterize the safety of treatment with fordadistrogene movaparvovec in participants in Cohort 2.	Incidence, severity and causal relationship of TEAEs (AEs and SAEs) after fordadistrogene movaparvovec administration through Year 2 Week 52. Incidence of abnormal laboratory findings and magnitude of change from pre-fordadistrogene movaparvovec baseline through Year 2 Week 52. Abnormal and clinically relevant changes from pre-fordadistrogene movaparvovec baseline through Year 2 Week 52 in: • Physical exam; • Neurologic exam; • Weight; • Vital signs; • ECG; • Echocardiogram; • Cardiac MRI • CBCL.
To characterize the long-term safety of treatment with fordadistrogene movaparvovec.	Incidence, severity and causal relationship of TEAEs (AEs and SAEs) through 5 years post fordadistrogene movaparvovec administration. Incidence of abnormal laboratory findings and magnitude of change through 5 years post fordadistrogene movaparvovec administration. Abnormal and clinically relevant changes through 5 years post fordadistrogene movaparvovec administration in: • Physical exam; • Neurologic exam; • Weight; • Vital signs; • ECG; • Echocardiogram; • Cardiac MRI • CBCL.

4. STUDY DESIGN

4.1. Overall 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 9.3), 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 approximately 55% of dosed participants are in either of the Screening age strata. 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.

In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post-IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits to the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. Ongoing blinded review of safety data will be conducted by the study team, and frequent periodic unblinded reviews of safety data will be conducted by the E-DMC, as described in detail in the E-DMC charter (see Section 9.5.1).

Table 1 provides a brief overview of the study periods; for full details please see SoA.

Table 1. Brief Overview of the Study Periods

Study Period	Days and Visits	Overview of Main Tests/Procedures
Study Eligibility Assessment	Screening (Visit 1)	Inclusion and Exclusion criteria review.
	Baseline (Visit 2)	Inclusion and Exclusion criteria review, including NAb results; Efficacy assessments; Muscle biopsy;* Obtain weight measurement; Randomization and request IP.
IP Administration	Day 1 (Visit 3)	Pre-dose Inclusion and Exclusion criteria review, including NAb results; Year 1 IP administration;
Post IP safety monitoring	Day 2 (Visit 4) to Day 34 (Visit 13)	Post-dose safety monitoring; Viral vector shedding.
Completion of Year 1	Day 60 (Visit 14) to Day 360 (Visit 19)	Routine safety monitoring; Efficacy assessments; Muscle biopsy (Day 360);* Obtain weight measurement (Visit 18);** Request IP on Day 328 (Visit 18); Viral vector shedding.
Eligibility Assessment for Year 2 IP Administration	Day 360 (Visit 19)	Assess eligibility for Year 2 IP administration, including NAb results. Viral vector shedding.
IP Administration	Day 390 (Visit 20)	Pre-dose review of eligibility for Year 2 IP administration, including NAb results; Year 2 IP administration.
Post IP safety monitoring	Day 391 (Visit 21) to Day 423 (Visit 30)	Post-dose safety monitoring; Viral vector shedding.
Completion of Year 2	Day 449 (Visit 31) to Day 749 (Visit 35)	Routine safety monitoring; Efficacy assessments; Viral vector shedding.
Long-Term Follow-up Year 3 to Year 6	Day 930 (Visit 36) to Day 2190 (Visit 43)	Routine safety monitoring; Efficacy assessments; Viral vector shedding; Muscle biopsy (Day 1830).*

Table 1. Brief Overview of the Study Periods

Study Period	Days and Visits	Overview of Main Tests/Procedures

* First ~15 participants (with the potential to collect a maximum of 33 if needed) from selected sites. The post-Baseline muscle biopsies will be performed on Day 360 and Day 1830.
** For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the study dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.

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. After the database has been released for the primary analysis, the study may become fully unblinded.

Investigators in Japan should see Section 10.10 (Appendix 10) for details on the interval between IP administration for consecutive participants.

4.2. Scientific Rationale for Study Design

4.2.1. Rationale for Inclusion of a Placebo Control Group

The purpose of this Phase 3 study is to evaluate the safety and efficacy of a single IV administration of fordadistrogene movaparvovec compared to placebo in participants with DMD. The results of this study will be used to support submission for registration of this therapy for treatment of DMD. There are several reasons that a placebo-controlled design is necessary to generate robust results. First, there is considerable variability in the disease progression and therefore improved function among treated participants can be attributed to fordadistrogene movaparvovec only when compared to participants randomized to placebo. Second, in the age range of the study population, some young participants may be improving their motor function as a result of ongoing development and the only way to differentiate this improvement from that which may occur as a result of fordadistrogene movaparvovec is by comparison to a placebo group. Third, there are not adequate data on the impact of small changes in glucocorticoid regimen, as are allowed in this study, to differentiate this effect from that of fordadistrogene movaparvovec. Ensuring that the study remains blinded through the primary analysis is important because knowledge of treatment assignment can bias performance and evaluation of functional assessments.

Those randomized to Cohort 2 will receive fordadistrogene movaparvovec after completing the first year of observation, provided they remain eligible. This will enable all eligible participants to receive treatment with fordadistrogene movaparvovec.

4.2.2. Rationale for Selected Participant Population

The selected population includes participants with a genetic diagnosis of DMD who are ambulatory and age ≥4 to <8 years. There are two observations underlying the rationale for this age range.

The first, which defines the upper age limit, is based on the pathophysiology of DMD and the mechanism of action of fordadistrogene movaparvovec. Lack of functional dystrophin leads to damage of the sarcolemma upon repeated muscle contraction. This initially causes inflammation followed by cell death with replacement of muscle by fibrosis and fat. The goal of gene therapy is to provide mini-dystrophin to skeletal and cardiac muscle such that it replaces the missing or dysfunctional endogenous dystrophin and acts to protect muscle, thereby significantly reducing the inflammatory and fibrotic processes. Muscles that have already progressed to cell death and fibrosis are not expected to be affected by therapy. Thus, it is anticipated that maximum benefit will occur for patients in whom there is minimal irreversible muscle damage. Imaging studies have revealed that some inflammation and fibrosis occurs in select lower limb muscles in patients as early as age 2 years (Li et al., 2015).[51] While most lower limb muscles have fatty infiltration by age 7 years, with the severity of fatty infiltration increasing rapidly after this age, different patients of the same age have varying degrees of fatty infiltration of the thigh muscles, ranging from mild to severe (Li et al, 2015).[51] These imaging findings correspond to the average pace of clinical disease progression in which initial symptoms often present at age 2 years, improvement in ambulatory motor function occurs as a result of development through age 5 years, a plateau in function persists through age 7 years, and then decline occurs until loss of ambulation at approximately age 12 years (Ciafaloni et al., 2009; Bushby & Connor, 2011; McDonald et al., 2013; Mercuri et al., 2016).[52,53,54,55] In order to minimize clinical heterogeneity and to treat boys prior to their anticipated functional decline, the designated age range for this trial has a maximum of <8 years old . However, as there is broad variability in DMD disease progression, and disease milestones will not occur at the same ages for all patients, there is the potential for treatment benefit outside of the age range included in the trial (Zambon et al, 2022; Bello et al, 2016)[56, 57].

The second observation, which defines the lower age limit, is based on the ability of the NSAA to reflect motor function across a range of ages. This endpoint was initially validated for DMD patients age ≥4 years [Mayhew et al., 2013; Scott et al., 2012; Mazzone et al., 2009].[58,59,60] There have been reports of the NSAA being used in patients as young as 3 years of age (DeSanctis et al., 2013; Mercuri et al. 2016).[61,55] However, it has been shown that typically developing boys cannot perform all the items until age 4 years (Mercuri et al., 2016),[55] and thus the full scale could not be used in boys below age 4 years. Furthermore, the development of motor skills prior to age 4 years in DMD boys can be affected by cognitive aspects of the disease that are not the target of therapy with fordadistrogene movaparvovec. Therefore, NSAA as a primary efficacy endpoint in this study is most appropriate with a population age ≥4 years.

4.2.3. Rationale for Selecting NSAA for the Primary Endpoint

There are multiple aspects of the NSAA that make it suitable as a primary efficacy endpoint in the ambulatory DMD population. First, it is a validated measure developed specifically for the DMD population in order to precisely monitor disease progression and the impact of potential treatments (Scott et al., 2012).[59] Second, substantial natural history collected over several different studies has revealed that it is sensitive enough to capture change in disease state over a one year period, and that the variability in this change is relatively small, such

that a study of reasonable sample size can be performed. By contrast, other measures used in the clinical trial setting to evaluate ambulatory DMD patients, such as the Six Minute Walk Test and the Four Stair climb, have been shown to have less change over one year and higher variability. Third, NSAA is capable of differentiating function in DMD patients from that in normally developing boys over the entire age range of this study (DeSanctis et al., 2015; Mercuri et al., 2016),[61,55] which is not the case with other measures of ambulatory function, such as the 10 meter run/walk and the Six Minute Walk Test. This aspect of the NSAA provides the potential to capture improvement in function (rather than simply stability) that may occur as a result of treatment. Finally, since the NSAA is comprised of several activities required for daily living, such as rising from the floor, standing, walking, and rising up onto a step, it is a comprehensive evaluation that best reflects the ability of boys to function in their daily lives. As such, it aligns with the potential value of therapy for patients and their caregivers, and with the interest of regulatory agencies to evaluate treatments utilizing endpoints that reveal the impact of therapy on daily living.

4.2.4. Rationale for Collection of Muscle Biopsies

This study includes open muscle biopsy procedures for approximately 15 study participants (with the potential to collect a maximum of 33 if needed) at three time points: at Baseline (Visit 2) and post-Baseline at Day 360 (Visit 19) and at Day 1830 (Visit 41). These biopsies will enable an assessment of the change from Baseline in the percent normal mini-dystrophin protein expression level and of the percent of muscle fibers expressing mini-dystrophin. Results of these analyses are important for 2 reasons. First, data on the expression and distribution of mini-dystrophin in skeletal muscle could enable a more thorough understanding of the elements contributing to the effects of treatment on function. Second, a demonstration in this study that mini-dystrophin expression is reasonably likely to predict clinical benefit could enable the use of this biomarker to support evidence of efficacy in other DMD populations in which functional endpoints are not as established.

4.2.5. Rationale for Collection of Banked Biospecimens

Banked biospecimens will be collected for exploratory pharmacogenomic, genomic, and/or biomarker analyses and retained in the Biospecimen Banking System (BBS), which makes it possible to better understand the IP's mechanism of action and to seek explanations for differences in, for example, exposure, tolerability, safety, and/or efficacy not anticipated prior to the beginning of the study.

4.3. Justification for Dose

At the initiation of the clinical program, 2 potentially safe and effective doses were identified through pre-clinical studies: 1E14 vg/kg and 3E14 vg/kg. The rat dose-finding study indicated that the minimal effective dose was 1E14 vg/kg wherein there was efficient muscle transduction and efficacy. The dose of 3E14 vg/kg was determined to be the NOAEL in a juvenile rat toxicology study and was associated with increased transduction and dystrophin expression in cardiac and skeletal muscles in the rat dose-finding study. The DMD rat model showed efficacy at both of these dose levels, with improvement of the tissue architecture of

skeletal muscles and heart, improved muscle strength and endurance, and improvement of the cardiac diastolic function.

As of 20 May 2019, the biceps brachii muscle biopsies in 3 participants in each of the low and high dose cohorts in Study C3391001 at Baseline and 2 months post-treatment have been evaluated for percent normal mini-dystrophin expression level and percent of muscle fibers expressing mini-dystrophin. The preliminary results provide evidence of transduction. Since the degree of functional benefit produced by specific mini-dystrophin expression levels is unknown, it was determined that using 3E14 vg/kg to enable a higher degree of mini-dystrophin expression would be most likely to produce the greatest clinical benefit. In addition, the safety profile of 3E14 vg/kg, as understood through the exposures in the Phase 1b study to date, appears to be adequate to support the benefit:risk of this dose.

The assay used to determine the dose for the Phase 1b study was based on the detection of the inverted terminal repeats (ITR) within the DNA sequence. The assay used to determine the dose for the Phase 3 study is based on the detection of the transgene (TG) DNA sequence, in accordance with regulatory requirements. The numerical results of these assays differ slightly such that a dose of 3E14 using the ITR method is approximately equivalent to a dose of 2E14 with the TG method. Therefore, the dose selected for Study C3391003, identified as 2E14, is approximately equivalent to the highest dose of 3E14 used in Study C3391001.

4.4. End of Study Definition

A participant is considered to have completed the study if he has completed all periods of the study including the last visit shown in the Schedule of Activities.

The end of the study is defined as the date of the last visit of the last participant in the study.

5. STUDY POPULATION

This study can fulfill its objectives only if appropriate participants are enrolled. The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular participant is suitable for this protocol.

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

1. Male participants who are ≥4 and <8 years of age at Screening (Visit 1).

2. Confirmed diagnosis of DMD by prior genetic testing demonstrating the presence of a mutation in the dystrophin gene consistent with DMD at Screening (Visit 1). If the

Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1).

3. Receipt of a stable daily dose of glucocorticoids (≥0.5 mg/kg/day prednisone, prednisolone, or ≥0.75 mg/kg/day deflazacort) for at least 3 months prior to Screening (Visit 1) and during the period between Screening (Visit 1) and Day 1 (Visit 3). In order to comply with protocol procedures, there should also be a reasonable expectation that this daily dose of glucocorticoids will remain stable for the first 2 years of the study. A stable dose is defined as one in which any change is ≤0.2 mg/kg (See Section 6.5.1 for detailed requirements).

4. A NSAA total score >16 and <30 at Screening (Visit 1).

5. Ambulatory, defined as being able to walk 10 meters unassisted, at Screening (Visit 1).

6. Participants/legally acceptable representatives who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures including, potentially, open muscle biopsies under general anesthesia and cardiac MRI under general anesthesia.

7. Participants/legally acceptable representatives who are capable of giving assent/signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the assent/informed consent document (ICD) and in this protocol.

8. Participants/legally acceptable representatives who are willing to protect the integrity of the study data by not actively seeking sensitive clinical data (eg, CK, ALT, AST, NAb to AAV9) through independent laboratory tests and by not sharing trial experiences with other participants or publicly (eg, through social media).

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

1. Prior treatment with gene therapy, defined as any therapy introducing exogenous DNA or intended to permanently alter the endogenous DNA. Gene therapy (other than IP) will be prohibited for the duration of the study.

2. Exposure within 6 months prior to Screening (Visit 1) to any treatment designed to increase dystrophin expression (including, but not limited to exon-skipping and nonsense read-through). These treatments will also be prohibited during the period

between Screening (Visit 1) and Day 1 (Visit 3) and for the first 52 weeks of the study. Please note that for participants who are eligible for these treatments:

Participants may be enrolled who have previously experienced lack of efficacy, or intolerance, as long as they received their last dose more than 6 months before screening (Visit 1), or who have refused these treatments.

Participants receiving these treatments from which there is believed to be benefit should not discontinue them in order to meet this exclusion criterion and enroll in the study.

3. Previous administration with an investigational drug or investigational vaccine within 30 days (or as determined by the local requirement) or 5 half-lives (whichever is longer) at Screening (Visit 1). These treatments will also be prohibited during the period between Screening (Visit 1) and Day 1 (Visit 3) and for the first 2 years of the study.

4. Known cognitive impairment or behavioral issues that would impede the ability to follow instructions, in the judgment of the Investigator, at Screening (Visit 1).

5. Any nonhealed injury at Screening (Visit 1) which, in the opinion of the Investigator, may impact functional testing; additionally, lower limb fractures must have been healed for at least 3 months prior to Screening (Visit 1).

6. Positive test for NAb to AAV9, based on the threshold determined by the Central Laboratory, from a sample taken at Screening (Visit 1).

7. Receipt of a live attenuated vaccination within 30 days prior to Screening (Visit 1). Receipt of a live attenuated vaccination will also be prohibited for 90 days before Day 1 (Visit 3), for 90 days prior to Year 2 IP administration, and for the first 2 months after each IP administration.

8. Abnormality in hematology or chemistry profiles at Screening (Visit 1). A single repeat for value(s) outside allowable limits is permitted to re-assess eligibility:

    a. Absolute neutrophil count <1000 cells/mm^3;

    b. Platelets <150 x $10^3/\mu l$;

    c. Cystatin C >1.2 x ULN;

    d. Positive hepatitis A virus (anti-HAV) immunoglobulin M, hepatitis B surface antigen (HbsAg), and/or hepatitis C antibody (HCVAb);

e. Markers of hepatic inflammation or overt or occult cirrhosis as evidenced by one or more of the following:

1. Prothrombin time (PT) > upper limit of normal (ULN); prolonged international normalized ratio (INR) >ULN;

2. GLDH >2 x ULN;

3. Total bilirubin >1.5 x ULN (unless the participant has a history of Gilbert disease) and direct bilirubin >0.5 mg/dL;

4. Gamma-glutamyl transferase (GGT) >1.5 x ULN.

9. Other acute or chronic medical or psychiatric condition at Screening (Visit 1), including recent (within the past year) or active suicidal ideation or behavior (using screening by the Child Behavior Check List (CBCL) and determined by the Investigator, as described in Section 8.2.13) or laboratory abnormality that may increase the risk associated with study participation or IP administration or may interfere with the interpretation of study results and, in the judgment of the Investigator, would make the participant inappropriate for entry into this study.

10. Acute infection at Screening (Visit 1) or Baseline (Visit 2) that, in the judgement of the Investigator is not expected to be fully resolved at least 2 weeks before Day 1 (Visit 3). At Day 1 (Visit 3), participants must have been infection-free for at least 2 weeks prior to IP administration. Delay of IP administration for up to 14 days is permitted to enable infections to become fully resolved.

11. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the Investigator, or Pfizer employees, including their family members, directly involved in the conduct of the study.

12. Known hypersensitivity to any of the components of the IP or solution for infusion, such as hypersensitivity to albumin or a diagnosis of HFI. Symptoms suggestive of HFI include nausea, vomiting, bloating, stomach cramps, or diarrhea following the ingestion of sweet foods or drinks, or a pattern of avoiding sweet foods or drinks.

13. Contraindication to the use of eculizumab, as per the local prescribing information.

14. LVEF <50% on echocardiogram performed at the Screening Visit (Visit 1), as evaluated by the central reader.

15. Participants with the following genetic abnormalities in the dystrophin gene as confirmed by the investigator based on the review of DMD genetic testing:

a. Any mutation (exon deletion, exon duplication, insertion, or point mutation) affecting any exon between exon 9 and exon 13, inclusive; OR

b. A deletion that affects both exon 29 and exon 30; OR

c. A deletion that affects any exons between 56-71, inclusive.

For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.

16. Cardiac pathologies, as evaluated by a pediatric cardiologist at the Screening Visit (Visit 1):

a. Diagnosis of myocarditis (eg, viral): either based on prior medical history or based on findings in cardiac imaging tests;

b. Any other cardiac history, and/or condition and/or abnormalities in cardiac imaging, that determine that the participant should not be included in the study, as per the cardiologist.

17. Not a candidate for mechanical cardiac or respiratory support, or any other invasive intervention, if indicated for management of an acute event as determined by the cardiologist in consultation with the investigator at the Screening Visit (Visit 1).

5.3. Management of Participants Post Enrollment and Dosing Pause

If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), the time between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), or the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20) is more than 90 days, participants will undergo one or more unplanned visits to repeat tests and procedures, as applicable to re-confirm study/IP administration eligibility criteria.

5.3.1. Study and Year 1 IP Administration Eligibility

If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), the time between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), is more than 90 days, participants will undergo an unplanned visit to repeat the following tests and procedures, as applicable, and will re-confirm all study/IP administration eligibility criteria:

- Full physical and neurological examination;
- Vital signs;
- Laboratory tests: clinical safety, chemistry and hepatic safety, cardiac troponin, INR, and hepatitis serology;
- NAb to AAV9, if the previous sample was collected more than 55 days before the day of IP administration (see Section 6.1.1);

- Functional assessments: NSAA, ambulatory status;
- Echocardiogram and ECG;
- Medical history, concomitant medications, and background glucocorticoid regimen assessment.
- Weight: for participants who were already randomized but have not yet received IP, weight will be measured again following the process outlined in Section 8.2.3. The site will update the weight in the IRT system, to allow re-calculation of the dose of IP if needed, once study eligibility is re-confirmed. Participants with an increase or decrease in body weight of more than 5% will have the dose of IP re-calculated.

If a participant has started or completed the Screening Visit (Visit 1), but was not yet randomized when the assessments are repeated, and he is found to be ineligible for study entry based on the results of repeated tests and procedures, he will be screen failed.

If a participant was already randomized, but had not yet received IP when the assessments are repeated, and he is found to be ineligible for study entry based on the results of the repeated tests and procedures, he will be withdrawn from the study.

For participants who completed the Baseline Visit (Visit 2) and were randomized, and who are re-confirmed to be eligible for study entry, a second unplanned visit will be scheduled to perform a NAb to AAV9 test if the Day 1 Visit (Visit 3) is expected to be more than 55 days after the collection of the previous sample.

5.3.2. Year 2 IP Administration Eligibility

If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. Participants with delayed Year 2 IP administration will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator), for sites in Israel, see Appendix 16.

At this visit the following tests and assessments will be performed:

- Full physical and neurological examination;
- Vital signs;

- Laboratory blood tests: clinical safety; chemistry and hepatic safety, troponin and CK;
- Functional assessments: NSAA, ROM, and ambulatory status;
- Echocardiogram and ECG.

Once the pause is lifted, participants who have attended Day 360 (Visit 19) more than 90 days before will undergo another unplanned visit to assess eligibility for IP administration. This visit will require the same tests and procedures as the Day 360 (Visit 19) (see Section 1.3.1). Additionally, sites will enter the weight measured at this unplanned visit into the interactive response technology drug management system to calculate the dose of IP for Year 2 administration and to trigger IP shipment to the site. Participants with an increase or decreased in body weight of more than 5% will have the dose of IP re-calculated

For participants who attended the prior unplanned visit for general monitoring within 90 days of the second unplanned visit to confirm eligibility for Year 2 IP administration, only the following laboratory tests will be performed:

- NAb to AAV9
- INR and hepatitis serology

For participants confirmed to be eligible for Year 2 IP administration by the unblinded medical monitor (see Section 7.1), Day 390 (Visit 20) should take place within 30 days of the unplanned visit. At this visit the investigator will review the additional Year 2 IP administration eligibility criteria (see Section 7.1) and confirm if the participant can receive IP. After Year 2 IP administration has taken place, participants will continue to follow the regular protocol Schedule of Activities; the days in study will be counted starting on the day of Year 2 IP administration.

5.4. 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 analyses of the primary and secondary endpoints, and thus siblings will not be included within the approximately 99 participants in the FAS (see Section 9.3) required to provide adequate power for the primary endpoint. Data from the sibling(s) will be included in a supplemental analysis of the primary endpoint, all analyses of safety, and in exploratory analyses of participants in Cohort 2 during the delayed treatment period (Change from pre fordadistrogene

movaparvovec Baseline to Year 2 Week 52) and of long-term efficacy (Change from pre fordadistrogene movaparvovec baseline at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration).

If the participant is randomized within the first approximately 15 participants collecting muscle biopsies, muscle biopsies will be collected from him and his sibling(s), but sibling(s) will not contribute to the approximately 15 participants. Biopsy data from the sibling(s) will be excluded from analyses of mini-dystrophin in this study but will be included in supplemental analyses of mini-dystrophin endpoints. Because of this, it may be necessary to perform more than 15 muscle biopsies at each time point to accrue muscle biopsies from approximately 15 participants.

The rationale for ensuring that the sibling(s) receives the same treatment as the participant is to minimize the risk that brothers are randomized to different cohorts and the one receiving placebo at Year 1 Day 1 develops NAb, due to close household contact with the one receiving fordadistrogene movaparvovec, and therefore cannot receive treatment at Year 2 Day 1.

5.5. Lifestyle Considerations

5.5.1. Activity

Participants should be instructed to continue with routine physical therapy including stretching and use of orthoses to prevent or minimize contractures or muscle deformities.

Participants will be instructed to maintain normal activity levels and avoid activities that are not part of their normal daily routine for 24 hours before study visits where functional assessments will be performed.

5.5.2. Hydration

In general, participants are recommended to drink at least 1 liter of fluid per day to stay hydrated, particularly in the first month following each IP administration and prior to all study visits.

In addition, for the first 34 days following each IP administration (or longer if deemed clinically necessary), participants should be monitored to determine if they pass urine at least once during a 12-hour period or if they have a significant change in urine output in less than 24 hours. If fluid intake and/or urine output are observed to be less than these thresholds, then participants (and/or caregivers) should be instructed to promptly contact the site for a possible unscheduled visit and/or biospecimen collection.

5.5.3. Hygiene

It is suggested that the participant and those around him be reminded to practice good hygiene, especially for the month prior to and during the first 2 months after each IP administration, such as the following: (1) thoroughly washing hands with soap and water after using the bathroom, before preparing or touching food, or after blowing one’s nose,

coughing, sneezing, etc.; (2) limiting contact with persons who might be sick; and (3) not sharing glasses, dishes, utensils, or other items that touch the mouth.

Families and close contacts of the participant should be made aware of the potential risk for developing NAbs to AAV9 for at least the first 2 months after IP administration, which is especially relevant for any contact who might be a candidate for gene therapy. The risk can be reduced by avoiding contact with the participant´s bodily fluids (such as saliva, urine, and blood) during at least the first 2 months after IP administration.

5.6. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomized to a cohort. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

If the 90-day period between the Screening Visit (Visit 1) and Day 1 Visit (Visit 3), or between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20) is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to identify clinically significant changes in key tests and assessments (see Section 5.3).

5.7. Caregiver(s)

The parent(s) or legal guardian(s) of the participant will actively participate as caregiver(s) in this study. As caregiver(s), the parent(s) or legal guardian(s) will not only provide informed consent, but will also actively participate in the study, including attendance at study visits and completion of clinical outcomes assessments regarding caregiver topics and on behalf of the participant. With consent, the caregiver's demographic information may be collected. The caregiver(s) will also communicate observed safety information to the Investigator or designee as appropriate.

A participant's caregiver(s) must meet all of the following criteria for the participant to be eligible for enrollment in the study:

- Aged ≥18 years and responsibility as a legal caregiver;
- Willingness and ability to provide written informed consent on behalf of the participant;
- Ability to accompany the participant to the clinic visits;
- Ability to follow instructions.

6. STUDY INTERVENTION

Study intervention is defined as any investigational intervention(s), marketed product(s), placebo, or medical device(s) intended to be administered to a study participant according to the study protocol.

For the purposes of this protocol, the term IP may be used synonymously with study intervention.

6.1. Study Intervention(s) Administered

Intervention Name	fordadistrogene movaparvovec	Placebo for fordadistrogene movaparvovec
Type	Gene Therapy	Placebo for Gene Therapy
Use	Experimental	Placebo
IMP and NIMP/AxMP	IMP	IMP
Dose Formulation	Sterile Solution for Infusion	Sterile Solution for Infusion
Unit Dose Strength(s)	1E14 vg/mL Note: This is the nominal concentration of the IP; for lot specific dosing calculation, the exact strength of each lot will be provided. For nominal dosing, 1E14 vg/mL will be the concentration used for the calculation of the administered dose. Nominal dosing will only be implemented for Year 2 IP administration. The Sponsor will communicate to the sites what dosing strategy must be implemented for each participant to be dosed. (Refer to IP Manual for further details)	0 vg/mL
Dosage Level(s)	2E14 vg/kg Single dose IV infusion	0 vg/kg Single dose IV infusion
Route of Administration	Intravenous Infusion	Intravenous Infusion
Sourcing	Provided centrally by the Sponsor (Refer to IP Manual for further details)	Provided centrally by Sponsor (Refer to IP Manual for further details)
Packaging and Labeling	Study intervention will be provided as 5 mL per vial (5 mL/vial). Each vial will be labeled as required per country requirement	Study intervention will be provided as 5 mL per vial (5 mL/vial). Each vial will be labeled as required per country requirement
SRSD	IB	IB

Study Intervention(s)						
Intervention Name	IV methylprednisolone	Oral prednisone or prednisolone	Deflazacort	Eculizumab	Antiemetics eg. ondansetron	MenACWY Vaccine
Type	Drug	Drug	Drug	Drug	Drug	Vaccine
Use	One-time, pre-administration of IP, Year 1 and Year 2	Background glucocorticoid regimen pre- IP administration and after completion of 90-day Protocol-mandated glucocorticoid regimen for at least the first 2 years in the study. Protocol-mandated post-IP dosing for 90 days	Background glucocorticoid regimen pre- IP administration and after completion of 90-day Protocol-mandated glucocorticoid regimen for at least the first 2 years in the study	Medication to treat adverse events (aHUS), to be administered at the discretion of the Investigator. Guidance for use provided in Section 6.5.1	Medication to prevent or treat adverse events (nausea and/or vomiting), to be administered at discretion of Investigator. See Section 6.5.1	Required per eculizumab label. Must be administered no later than 30 days before and only after 60 post- IP administration. See Section 6.5.1
IMP or NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP
Dose Formulation	Sterile solution for injection	Tablets or Oral Suspension	Tablet or Oral suspension	Sterile Solution for Infusion	Orally disintegrating tablet or sterile solution for injection	Solution for injection
Unit Dose Strength(s)	40 mg/mL	1 mg, 2 mg or 5 mg	Tablets: 6 mg, 18 mg, 30 mg or 36 mg Oral Suspension: 22.75 mg/mL	300 mg concentrate (10 mg/ml)	Tablet: 4 mg or 8 mg Injection: 2mg/mL	10 mcg group A, 5 mcg group C, 5 mcg group W-135, 5 mcg group Y

Study Intervention(s)						
Dosage Level(s)	2 mg/kg	At least 0.5 mg/kg/day	At least 0.75 mg/kg/day	Total dose to be determined by the investigator	Total dose to be determined by the investigator	Single dose injection (0.5mL)
Route of Administration	Intravenous infusion	Oral	Oral	Intravenous Infusion	Oral/ injection/IV infusion	Intramuscular injection
Sourcing	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	The sponsor will provide initial safety stock then remaining supply to be sourced by the clinical site using locally approved product unless otherwise arranged with the sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor
Packaging and Labeling	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as 300 mg/30mL (10mg/mL) vial concentrated solution for intravenous infusion. Product will be labeled as required per country and site requirements.	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements
SRSD	SmPC	SmPC	SmPC	SmPC	SmPC	SmPC

Of the study interventions listed in the table above: IV methylprednisolone, oral prednisone, or prednisolone, deflazacort, eculizumab, antiemetics e.g., ondansetron and MenACWY vaccine are not subject to safety reporting in accordance with Japanese regulation requirements. Please refer to Section 10.10 (Appendix 10).

For investigators in Japan, please refer to Section 10.10 (Appendix 10) for the reporting of study intervention defects.

6.1.1. Administration

PLEASE NOTE: Participants will not receive IP if they meet any of the following; (for Year 2 IP administration eligibility, please see Section 7.1).

1. Receipt of a treatment with gene therapy, defined as any therapy introducing exogenous DNA or intended to permanently alter the endogenous DNA between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3). Participants who receive a treatment with gene therapy between Screening (Visit 1) and Day 1 (Visit 3) will not be eligible for IP administration and will be withdrawn from the study.

2. Receipt of a treatment designed to increase dystrophin expression (including, but not limited to exon-skipping and nonsense read-through) between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3). Participants who receive a treatment designed to increase dystrophin expression between Screening (Visit 1) and Day 1 (Visit 3) will not be eligible for IP administration and will be withdrawn from the study.

3. Receipt of an investigational drug or investigational vaccine between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3). Participants who receive an investigational drug or investigational vaccine between Screening (Visit 1) and Day 1 (Visit 3) will not be eligible for IP administration and will be withdrawn from the study.

4. Positive test for NAb to AAV9, based on the threshold determined by the Central Laboratory, at Baseline (Visit 2); if the analysis of NAb to AAV9 was required due to the first blood draw for NAb to AAV9 testing at the Day 1 (Visit 3), or most recent test, if repeat blood draw(s) was required, being more than 55 days after the Screening Visit (Visit 1), please see Section 1.3.1. Participants who have a positive test for NAb to AAV9 will be withdrawn from the study.

5. Receipt of a live attenuated vaccination within 90 days prior to Day 1 (Visit 3). If a participant has received a live attenuated vaccination within 90 days prior to Day 1 (Visit 3), IP administration must be delayed until at least 90 days after the last administration of the vaccine.

6. Receipt of an inactivated vaccine (eg, influenza, meningococcus, pneumococcus, Haemophilus influenzae vaccination) within 30 days prior to Day 1 (Visit 3). If a participant has received an inactivated vaccine within 30 days prior to Day 1 (Visit

3), IP administration must be delayed until at least 30 days after the last administration of the vaccine.

7. Receipt of an mRNA or DNA-based, or non-replicating viral vector vaccine (eg, against SARS-CoV2) within 30 days prior to Day 1 (Visit 3). If a participant has received any of the above-listed vaccines within 30 days prior to Day 1 (Visit 3), IP administration must be delayed until at least 30 days after the last administration of the vaccine.

8. Receipt of any systemic immunosuppressant agents other than glucocorticoids, and/or, systemic antiviral, and/or interferon therapy. If a participant has received any of the above-listed therapies within 30 days prior to Day 1 (Visit 3), IP administration must be delayed until at least 30 days after the last dose.

9. Acute infection at Day 1 (Visit 3). At Day 1 (Visit 3), participants must have been infection-free for at least 2 weeks. Delay of IP administration for up to 14 days is permitted to enable infections to become fully resolved.

10. Participants with a myocarditis diagnosed by a pediatric cardiologist between Screening (Visit 1) and Day 1 (Visit 3) will not be eligible for IP administration and will be withdrawn from the study.

Per the treatment assignment dosing schedule, participants will be admitted to the site to receive a single intravenous infusion of IP delivered over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush), at a rate no more than 125 mL/hour, at Day 1 (Visit 3) and Day 390 (Visit 20), in accordance with the Schedule of Activities, and will be monitored as described in Section 8.2.10.

In lieu of their background glucocorticoid regimen, participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone, 1 to 4 hours prior to infusion of IP, followed by the protocol mandated glucocorticoid regimen for 3 months, as described in Section 6.5.1.

IP shipment will be initiated once the body weight is entered into the interactive response technology drug management system. The appropriate amount of IP, based on the actual concentration for the lot and participant's body weight (at Baseline (Visit 2) for Year 1 IP administration and at Day 328 (Visit 18) for Year 2 IP administration), will be prepared and administered in a solution of approximately 250 to 500 mL containing 1.25% human serum albumin. Appropriate medication and other supportive measures for management of an unexpected reaction to the infusion should be available in accordance with local guidelines.

For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the study dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.

Administration of IP should be performed by appropriately qualified, Good Clinical Practice (GCP)-trained, and preferably gene therapy-experienced members of the study staff (eg, physician, nurse, physician's assistant, or nurse practitioner) as allowed by local, state, and institutional guidance. Individuals allowed in the infusion room during IP administration should be limited to caregivers, the treating physician, and those involved in IP administration. All individuals present during administration should wear appropriate personal protective equipment as applicable per local practice.

The entire contents of the IV bag containing the investigational product solution should be administered intravenously, and subsequently the line should be flushed with 0.45% Sodium Chloride Injection (same as diluent used for dose preparation) in accordance with local site policies and procedures to ensure complete delivery of the dose and that a closed system is maintained to reduce risk for all individuals present during administration.

Should participants experience any infusion reaction during the IV infusion period, the administration should be interrupted. If the participant has mild signs or symptoms only at the site of the IV line, such as pain, and/or, redness of the skin, and/or itching, it is recommended that the Investigator assess the infusion reaction and establish a new IV access if needed, as every reasonable effort should be made to complete the entirety of the dose. If the participant presents signs or symptoms compatible with a systemic allergic reaction, the infusion should be immediately stopped, and supportive care provided according to the Investigator's standard of care practice. Signs or symptoms suggestive of a systemic allergic reaction may include: respiratory compromise such as dyspnea, wheeze-bronchospasm, stridor, hypoxemia; generalized cutaneous reaction (eg, generalized hives, itch-flush, swollen lips, tongue, uvula); reduced blood pressure or associated symptoms such as collapse, syncope or incontinence and/or persistent gastrointestinal symptoms such as abdominal pain and/or vomiting.[62]

The IP solution has 8-hour stability at room temperature from the start of dose preparation (initial IP vial puncture). The 8-hour in-use period cannot be extended, so if there is an interruption to the infusion, every effort should be made to resume and complete the infusion within this period. The investigator should establish new IV access, if needed, and complete the infusion provided participant safety is not compromised. The time at which the infusion was paused, the volume infused prior to pausing the infusion, and the time at which the infusion resumes should all be noted in source documentation by those involved in IP administration in addition to documentation required at end of infusion.

6.2. Preparation/Handling/Storage/Accountability

1. The Investigator or designee must confirm that appropriate temperature conditions have been maintained during transit for all study interventions received and that any discrepancies have been reported and resolved before use of the study intervention, as applicable for temperature monitored shipments.

2. Only participants enrolled in the study may receive study intervention and only authorized site staff may supply, prepare, or administer study intervention. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated recording) area in accordance with the labeled storage conditions with access limited to the Investigator and authorized site staff. At a minimum, daily minimum and maximum temperatures for all IP storage locations must be documented during which the IP is stored on site and available upon request. Data for nonworking days must indicate the minimum and maximum temperatures recorded by automated record devices, since it was previously documented for all site storage locations upon return to business.

3. The Investigator, institution, or the head of the medical institution (where applicable) is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records). All study interventions will be accounted for using an IP accountability form/record.

4. Further guidance and information for the final disposition of unused study interventions are provided in the IP manual.

5. Any storage conditions stated in the IP manual will be superseded by the storage conditions stated on the product label.

6. Study interventions should be stored in their original containers and in accordance with the labels.

7. See the IP manual for storage conditions of the study intervention once diluted.

8. Any excursions from the IP label storage conditions should be reported to Pfizer upon discovery along with any actions taken. The site should actively pursue options for returning the study intervention to the storage conditions described in the labeling, as soon as possible. Once an excursion is identified, the study intervention must be quarantined and not used until Pfizer provides permission to use the study intervention. It will not be considered a protocol deviation if Pfizer approves the use of the study intervention after the temperature excursion. Use of the study intervention prior to Pfizer approval will be considered a protocol deviation. Specific details regarding the definition of an excursion and information the site should report for each excursion will be provided to the site in the IP manual.

9. The Sponsor or designee will provide guidance on the destruction of used and unused study intervention (eg, at the site) in the IP manual. If destruction is authorized to take place at the Investigator site, the Investigator must ensure that the materials are destroyed in compliance with applicable environmental regulations, institutional policy, and any special instructions provided by Pfizer, and all destruction must be adequately documented.

Additional details about accountability, storage, destruction, and excursion reporting can be found in the IP manual.

6.2.1. Preparation and Dispensing

The amount of IP shipped to the site will be based on the participant's body weight measured at the Baseline Visit (Visit 2) for Year 1 IP administration and at Day 328 Visit (Visit 18) for Year 2 IP administration, and on the and IP concentration per vial. Approximately 14 to 45 days, depending on the site location, is required for shipment of IP.

For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the study dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.

The IP will be dispensed using an interactive response technology (IRT) drug management system for the dosing visits. A qualified staff member will dispense the IP via unique container numbers on the vials provided, in quantities appropriate for individual participant dosing once the participant is confirmed to be eligible for IP administration and admitted to the site for dosing.

Preparation of IP should be performed by appropriately qualified, Good Clinical Practice (GCP)-trained, and preferably gene therapy-experienced pharmacist as allowed by local, state, and institutional guidance. It is strongly recommended to prepare the IP dosing solution as close to the administration time on the dosing day as possible. See the IP manual for instructions on how to prepare the IP for administration. The IP manual will need to be reviewed and acknowledged by any site staff preparing and/or administering the product.

IP will be prepared by qualified blinded site personnel according to the IP manual. The IP will be administered to participants in a blinded fashion.

Only qualified personnel who are familiar with procedures that minimize undue exposure to themselves and to the environment should undertake the preparation, handling, and safe disposal of gene therapy agents. Please refer to the IP manual for detailed handling instructions.

6.3. Measures to Minimize Bias: Randomization and Blinding

6.3.1. Allocation to Investigational Product

Eligible participants will be randomized into Cohort 1 or Cohort 2 (See Section 4.1) in a 2:1 fashion, using the method of permuted blocks within each randomization strata, where the strata are defined by their age at Screening (<6 or ≥6 years old) with no more than approximately 55% of dosed participants in either of the Screening age strata. 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. The randomization schedule is generated by the Sponsor. Personnel who are directly involved in the study conduct are blinded to the randomization schedule.

Allocation of eligible participants to study intervention (see Section 4.1 for additional details) will proceed through the use of an IRT system. The site personnel (study coordinator or specified designee) will be required to enter or select information including, but not limited to, the user's identification (ID) and password, the protocol number, and the participant number. The IRT system will provide a confirmation report containing the participant number, randomization number, and container numbers assigned. The confirmation report must be stored in the site's files.

The eligible sibling(s) 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 (see Section 5.3) and study intervention for the sibling(s) will be manually assigned in the system by the IRT support team. Siblings will receive their own unique participant number.

IP will be dispensed at the study visits summarized in the SoA.

The study specific IRT reference manual will provide the contact information and further details on the use of the IRT system.

6.3.2. Breaking the Blind

The participants, Sponsor, vendors, and study personnel will be blinded to treatment allocation, except for an unblinded, medically-qualified monitor (medical monitor), independent from the team conducting and monitoring the study as defined in Section 7.1.

The IRT will be programmed with blind breaking instructions. In case of an emergency, the Investigator has the sole responsibility for determining if unblinding of a participant's treatment assignment is warranted. Participant safety must always be the first consideration in making such a determination. If the Investigator decides that unblinding is warranted, the Investigator should make every effort to contact the Sponsor prior to unblinding a participant's treatment assignment unless this could delay further management of the participant. If a participant's treatment assignment is unblinded, the Sponsor must be notified by the Investigator within 24 hours after breaking the blind. The date and reason that the blind was broken must be recorded in the source documentation and case report form

(CRF)/data collection tool (DCT). Unblinding will not necessarily lead to study discontinuation.

The study specific IRT reference manual will provide the contact information and further details on the use of the IRT system to break the blind.

6.3.3. Sensitive Clinical Data

Select safety and immunogenicity results

In order to prevent the functional unblinding of the treatment assignment, the results of the following assessments will not be shared with the study team or the site after Year 1 IP administration and throughout the blinded portion of the study:

- CK;
- AST and ALT;
- NAb to AAV9 (See Section 7.1);
- ELISpot to AAV9 and mini-dystrophin;
- ADA to AAV9 and mini-dystrophin;
- C3 and C4.

An unblinded medically qualified monitor (medical monitor) will review the results of CK, AST and ALT, NAb to AAV9, and ADA to mini-dystrophin for each participant on an ongoing basis and will decide if any result(s) should be repeated and/or shared with the site and the study team, due to a judgement that the results could reflect a safety issue (eg, liver injury, myositis, other immunological reaction).

If a participant in Cohort 2 presents with a positive test for NAb to AAV9 on the sample taken at the Day 34 (Visit 13) he will be withdrawn from the study given that it would already be determined at that time that he is not be eligible for fordadistrogene movaparvovec administration at Year 2. If this situation occurs while the study is still accruing participants, an additional 2 participants may be randomized for each Cohort 2 participant who is withdrawn.

Additionally, if the threshold of laboratory abnormalities for a potential drug-induced liver injury (DILI) case has been met (see Appendix 6), the results for ALT and AST will be shared with the site and the study team until the potential DILI has been investigated and it is considered resolved.

If a clinical event occurs that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction, additional ad-hoc assessments of NAb to AAV9, ADA to AAV9 and mini-dystrophin, ELISpot to AAV9 and mini-dystrophin may be conducted if

considered indicated by the Sponsor and/or the Investigator for the interpretation and/or the management of the immunological reaction. The results of these tests will be shared with the site and the study team.

Additionally, to further prevent the introduction of bias in the scoring of the functional assessments, all possible measures should be put into place to prevent the clinical evaluators from viewing the participants´ medical records/database where relevant information that could lead to functional unblinding, such as the occurrence of lab abnormalities or AEs/SAEs, may be recorded.

Viral vector shedding results

In order to prevent the functional unblinding of the treatment assignment, the results of the following assessments will not be shared with the site or the study team throughout the blinded portion of the study:

- Viral vector shedding.

An unblinded qualified Sponsor representative, independent and firewalled from the study team, will review the viral vector shedding results for each participant on an ongoing basis. The unblinded qualified Sponsor representative will communicate to the site when sampling in a given matrix (ie, blood, urine, or saliva) for each participant can be stopped. For Cohort 1 participants sampling for each matrix will be stopped when two consecutive samples test negative. To prevent unblinding, sampling will also be stopped for a matched Cohort 2 participant.

Muscle biopsy results

In order to prevent the functional unblinding of the treatment assignment, the results of the following assessments will not be shared with the site or the study team throughout the blinded portion of the study:

- Percent normal mini-dystrophin expression level, quantified by LC-MS.
- Percent of muscle fibers expressing mini-dystrophin, assessed by immunohistochemistry.

No review of these results will be conducted by the unblinded medical monitor.

Year 2 IP eligibility laboratory results

Given that the below eligibility assessment does not apply to Cohort 1 for Year 2 IP administration and in order to prevent unblinding of the treatment assignment, when assessing Cohort 2 participants' eligibility for Year 2 IP administration, the following test

results will not be shared with the sites and the study team, and will only be reviewed by an unblinded medical monitor (see Section 7.1).

- Laboratory results at Day 360 (Visit 19):

  NAb to AAV9;

  Absolute neutrophil count <1000 cells/mm^3;

  Platelets <150 x $10^3/\mu l$;

  Cystatin C >1.2 x ULN;

  Positive hepatitis A virus (anti-HAV) immunoglobulin M, hepatitis B surface antigen (HbsAg), and/or hepatitis C antibody (HCVAb);

  Markers of hepatic inflammation or overt or occult cirrhosis as evidenced by one or more of the following:

  - PT > ULN; prolonged INR >ULN;
  - GLDH >2 x ULN;
  - Total bilirubin >1.5 x ULN (unless the participant has a history of Gilbert disease) and direct bilirubin >0.5 mg/dL;
  - GGT >1.5 x ULN.

6.4. Study Intervention Compliance

The IP will be administered by the appropriately designated study staff at the Investigator site.

6.5. Concomitant Therapy

6.5.1. Permitted Therapies

Background glucocorticoid regimen (daily dose of ≥0.5 mg/kg/day prednisone or prednisolone, or ≥0.75 mg/kg/day deflazacort). There should be no changes to the background glucocorticoid regimen in the first two years of the study, except as described for the protocol-mandated glucocorticoid regimen, below. A change to the glucocorticoid regimen is defined as:

- A change >0.2 mg/kg in daily dose;
- A change in the specific glucocorticoid (prednisone, prednisolone, or deflazacort);
- A change in regimen (ie, from daily to any non-daily).

This definition also applies during the 3 months before the Screening Visit (Visit 1).

After two years (Day 749), any change to the background glucocorticoid regimen will be permitted.

Protocol-mandated glucocorticoid regimen for Year 1 and Year 2: to mitigate the risk of an immune response, participants will temporarily replace their background glucocorticoid regimen as follows:

1. Between 1 and 4 hours prior to IP administration: single dose of IV methylprednisolone 2 mg/kg. **Note:** Participants must be instructed to not take their background glucocorticoid dose on Day 1 (Visit 3) and on Day 390 (Visit 20).
2. From 1 to 15 days post-IP administration: 2 mg/kg/day oral prednisone or prednisolone.
3. From 16 to 30 days post-IP administration: 1.5 mg/kg/day oral prednisone or prednisolone.
4. From 31 to 60 days post-IP administration: 1.0 mg/kg/day oral prednisone or prednisolone.
5. From 61 to 90 days post-IP administration: 0.75 mg/kg/day oral prednisone or prednisolone.

A temporary increase in the daily dose of glucocorticoids, protocol mandated or background regimen, will be allowed only if medically required, after consultation with the Sponsor.

Following IP administration, participants with vomiting who cannot tolerate oral medications can receive IV glucocorticoids instead of oral glucocorticoids, per the clinical judgement of the Investigator. The dose of IV glucocorticoids must be consistent with the requirements of the protocol. The participants must return to oral glucocorticoids as soon as the Investigator considers that it is safe to do so.

Participants may return to their background glucocorticoid regimen after 90 days post-IP administration as long as there is no immune response or other clinical indication.

Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen in Year 2 and will continue receiving their background glucocorticoid treatment during Year 2, see Appendix 12 and Section 7.2.1.

Participants with delayed Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then, see Section 5.3.2.

Eculizumab

Treatment with one or more doses of the complement inhibitor, eculizumab, should be considered by the Investigator, according to the local prescribing information, for any participant who presents with a clinical picture of complement-mediated thrombotic microangiopathy. Signs consistent with atypical hemolytic uremic syndrome (aHUS) that would indicate the need for treatment include:

1. Creatinine >2 x Screening value; OR
2. Platelets <75 x 10^3/µl AND either (a) or (b):
    a. Evidence of hemolysis:
        - Haptoglobin <LLN or reduced to <50% from Screening value (Year 1) or from Visit 19 value (Year 2); or
        - Schistocytes on blood smear.
    b. Evidence of nephropathy:
        - Anuria >12 hours; or
        - ≥2+ blood or protein on urine dipstick; or
        - An increase of >50% in serum creatinine from Screening value.

Because the use of eculizumab increases the risk of contracting serious meningococcal infections, participants who have no contraindications and who have not previously received a vaccination against meningococcus or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer must receive at least one dose of meningococcal conjugate (MenACWY) vaccine as early as possible in the Screening Period and not later than 30 days before IP administration. If they receive eculizumab, and depending on the duration of the treatment with eculizumab, a decision will be made as to whether they should receive a second dose of meningococcal vaccination or antibiotic prophylaxis, at the discretion of the Investigator. Participants must also receive serogroup B meningococcal (MenB) vaccination if indicated by national vaccination guidelines. The Investigator must evaluate the immunization status against meningococcus and any other locally required immunization for all participants at Screening (Visit 1); local eculizumab prescribing information, including additional vaccination, and other requirements must also be followed as needed. Additionally, all sites must have the MenACWY vaccine, MenB vaccine (if recommended in the national vaccination guidelines) and eculizumab available for all participants (eculizumab should be available for the first 2 months after IP administration at Year 1 and at Year 2). For participants who cannot receive meningococcal vaccination, antibiotic coverage must be provided simultaneously with eculizumab.

Participants who experience an event compatible with aHUS may be screened for a genetic predisposition to aHUS, as determined by the Investigator in consultation with the Sponsor to increase the understanding of the risk of developing aHUS (see Appendix 2).

Antiemetics

At the discretion of the Investigator, participants may be administered an oral antiemetic such as oral ondansetron following IP administration and following the local prescribing information to prevent or treat symptoms of nausea and vomiting. Participants (and/or caregivers) should be instructed to contact the site if vomiting continues despite anti-emetic treatment. If required, an IV antiemetic such as ondansetron may be administered by the site.

Anesthesia

Participants will also receive anesthesia according to the site standard of care for the muscle biopsies obtained in this study.

Vaccines

Participants will be able to receive any required live attenuated vaccine(s) only during the following periods:

1. Up to 90 days before Day 1 (Visit 3).
2. Day 60 (Visit 14) to Day 300. In addition, participants in Cohort 1 confirmed to meet exclusion criterion 15 will be allowed to receive any required live attenuated vaccine(s) for the remainder of the study. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.
3. Day 450 until the end of the study.

Participants will be able to receive an inactivated vaccine (eg, influenza, meningococcal, pneumococcal, Haemophilus influenzae) only during the following periods:

1. Up to 30 days before Day 1 (Visit 3)
2. Day 60 to Day 360 (Visit 19). In addition, participants in Cohort 1 confirmed to meet exclusion criterion 15 will be allowed to receive any required inactivated vaccine(s) for the remainder of the study. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.
3. Day 450 until the end of the study.

Participants will be able to receive an mRNA, or DNA-based, or non-replicating viral vector vaccine (eg, against SARS-CoV2) only during the following periods:

1. Up to 30 days before Day 1 (Visit 3)

2. Day 60 to Day 360 (Visit 19). In addition, participants in Cohort 1 confirmed to meet exclusion criterion 15 will be allowed to receive any required mRNA, or DNA-based, or non-replicating viral vector vaccine(s) (eg, against SARS-CoV2) for the remainder of the study. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.

3. Day 450 until the end of the study.

Other medications

With the exception of any prohibited therapies, other medications may be used if deemed necessary by the Investigator.

6.5.2. Prohibited Therapies

The following therapies are prohibited from the time of signing the informed consent until the end of Year 2. After Day 749 (Visit 35) participants will be able to receive any of the therapies listed below, if deemed necessary. For Cohort 1 participants confirmed to meet exclusion criterion 15 and for participants who declined Year 2 IP administration (see Section 7.2.1), the medications listed below will be prohibited only until the end of Year 1. After Day 360 (Visit 19) these participants will be able to receive any of the therapies listed below, if deemed necessary. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.

1. **Immunosuppressant agents** (other than glucocorticoids, see Section 6.5.1) unless administered in response to immunologic reaction.

2. **Investigational therapies**, including those being evaluated for the treatment of DMD (eg, idebenone, tamoxifen).

3. **Antiviral therapy**, unless administered to treat an acute viral infection (eg, COVID-19).

4. **Interferon therapy**, unless administered to treat an acute viral infection and the participant is at least 2 months post IP administration.

Any therapy designed to increase dystrophin expression (including, but not limited to exon skipping and nonsense read-through) will be prohibited during the first 52 weeks of the study. When participants have completed Day 360 (Visit 19), if the Investigator determines that, due to worsening of DMD, an approved therapy with this mechanism were deemed necessary, such therapy would then be allowed.

Gene therapy, defined as any therapy introducing exogenous DNA or intended to permanently alter the endogenous DNA, will be prohibited from the signing of the informed consent until the end of the study.

6.5.3. Rescue Medicine

Not applicable.

6.6. Dose Modification

Not applicable.

6.7. Intervention After the End of the Study

No intervention will be provided to study participants at the end of the study.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

In the context of this study, treatment will consist of two single intravenous infusions, one of fordadistrogene movaparvovec and one of placebo (Section 4.1). Following IP administration on Day 1 (Visit 3), the only potential for discontinuation of study intervention is at the time of IP administration in Year 2. Cohort 1 participants will receive placebo on Day 390 (Visit 20) and will not be discontinued from study intervention although the timing of IP administration may be affected by eligibility criteria, as described below, in order to preserve the blinding of the ongoing study. Cohort 2 participants are scheduled to receive fordadistrogene movaparvovec one year after receiving placebo if they remain eligible for Year 2 IP administration. Participants in Cohort 2 who are determined to be ineligible to receive fordadistrogene movaparvovec by the criteria listed below (1-6) will discontinue study intervention.

Cohort 2 participants will be confirmed to be eligible for Year 2 IP administration before receiving treatment with fordadistrogene movaparvovec. There are no eligibility criteria for Cohort 1 participants for Year 2 IP administration based on the results of hematology and chemistry profiles or of results of testing for NAb to AAV9, but they will be reviewed for safety reasons. In order to preserve the blinding of the ongoing study, an unblinded, medically qualified monitor (medical monitor), independent from the team conducting and monitoring the study, will be the only person to review the results of the hematology and chemistry profiles as well as of the NAb to AAV9. These laboratory results will be blinded to the site and the Sponsor.

Additionally, the unblinded medical monitor will determine if any test(s) should be repeated (due to a result outside of allowable limits for Year 2 IP administration eligibility considered possibly transient for Cohort 2 participants, and/or due to test showing a potential safety issue considered possibly transient for Cohort 1 and Cohort 2 participants). The unblinded medical monitor will also decide if any result(s) must be unblinded to the site and the Sponsor, in the unlikely event that it reflects a safety issue.

Cohort 2 participants will not be eligible for Year 2 IP administration if they present with any of the following:

1. Positive test for NAb to AAV9, based on the threshold determined by the Central Laboratory, at Day 360 (Visit 19). If the time between Day 360 (Visit 19) and Day 390 (Visit 20) is more than 55 days, a second NAb to AAV9 test must be performed and confirmed to be negative before Year 2 IP administration. Dosing cannot occur unless there is a negative NAb to AAV9 test from a sample collected 55 or less days before the day of IP administration, as reviewed by the unblinded medical monitor.

2. Abnormality in hematology or chemistry profiles at Day 360 (Visit 19). A single repeat for value(s) outside allowable limits is permitted to re-assess eligibility:

   Absolute neutrophil count <1000 cells/mm^3;

   Platelets <150 x $10^3/\mu l$;

   Cystatin C >1.2 x ULN;

   Positive hepatitis A virus (anti-HAV) immunoglobulin M, hepatitis B surface antigen (HbsAg), and/or hepatitis C antibody (HCVAb);

   Markers of hepatic inflammation or overt or occult cirrhosis as evidenced by one or more of the following:

   - PT > ULN; prolonged INR >ULN;
   - GLDH >2 x ULN;
   - Total bilirubin >1.5 x ULN (unless the participant has a history of Gilbert disease) and direct bilirubin >0.5 mg/dL;
   - GGT >1.5 x ULN.

Additionally, the unblinded medical monitor will confirm the treatment allocation for participants with the conditions listed below, so those participants in Cohort 2 who meet any of these conditions do not receive Year 2 IP administration and are withdrawn from the study:

3. Participants screened or randomized who had not yet received Year 2 IP administration and were retrospectively confirmed to meet exclusion criterion 15 (see Appendix 12).

4. LVEF <50% on echocardiogram performed at Day 360 (Visit 19), or at the unplanned visit to re-assess eligibility for Year 2 IP administration.

5. Diagnosis of current or prior myocarditis by a pediatric cardiologist.

6. Not a candidate for mechanical cardiac or respiratory support, or any other invasive intervention, if indicated for management of an acute event as determined by the cardiologist in consultation with the investigator.

Cohort 1 participants, as confirmed by the unblinded medical monitor, will not receive Year 2 IP administration, placebo, if they meet exclusion criterion 15. They will not require post-IP safety monitoring in Year 2, will not attend Visit 18 in Year 1 and Visits 20 to 30.2 in Year 2, and will not receive their protocol-mandated glucocorticoid regimen in Year 2. These participants will remain in the study for safety monitoring as described in Appendix 12.

Once the unblinded medical monitor has communicated to the Investigator that the participant meets eligibility criteria based on laboratory tests and echocardiographic results, then the Investigator will ensure that none of the criteria listed below are met before allowing IP administration.

To preserve the blinding of the treatment assignment for the site and for the Sponsor, the following criteria will be assessed for both Cohort 1 and Cohort 2 participants.

7. Receipt of a live attenuated vaccination within 90 days prior to Day 390 (Visit 20). If a participant has received a live attenuated vaccination within 90 days prior to Day 390 (Visit 20), IP administration must be delayed until at least 90 days after the last administration of the vaccine.

8. Receipt of an inactivated vaccine (eg, influenza, meningococcal, pneumococcal, Haemophilus influenzae vaccination) within 30 days prior to Day 390 (Visit 20). If a participant has received an inactivated vaccine within 30 days prior to Day 390 (Visit 20), IP administration must be delayed until at least 30 days after the last administration of the vaccine.

9. Receipt of an mRNA or DNA-based, or non-replicating viral vector vaccine (eg, against SARS-CoV2) within 30 days of Day 390 (Visit 20). If a participant has received any of the above-listed vaccines within 30 days prior to Day 390 (Visit 20), IP administration must be delayed until at least 30 days after the last administration of the vaccine.

10. Receipt of any systemic immunosuppressant agents other than glucocorticoids, and/or systemic antiviral therapy, and/or interferon. If a participant has received any of these therapies, IP administration must be delayed until at least 30 days after the last dose.

11. Acute infection at Day 360 (Visit 19) that, in the judgement of the Investigator, is not expected to be fully resolved at least 14 days prior to IP administration on Day 390 (Visit 20).

12. Additionally, any participant, in Cohort 1 or Cohort 2, who has received gene therapy (other than IP) after Year 1 IP administration will not be eligible for Year 2 IP administration but will not be withdrawn from the study.

If any of the above eligibility criteria (7-11) are met for Cohort 1 or Cohort 2 participants, IP administration will be delayed until none of the criteria are met. If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20).

If a Cohort 2 participant is determined to be *permanently* ineligible for Year 2 IP administration, because of a confirmed result for the hematology or chemistry profiles outside allowable limits or because of a positive test for NAb to AAV9, based on the threshold determined by the Central Laboratory, he will be withdrawn from the study. The medical monitor will inform the site of the decision, to allow the site to communicate with the participant and the caregiver. In this circumstance, no Early Discontinuation Visit will be required.

7.1.1. Temporary Discontinuation

Not applicable.

7.1.2. Rechallenge

Not applicable.

7.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at his own request.

Reasons for discontinuation from the study include the following:

- Refused further follow-up;
- Lost to follow-up;
- Death;
- Study terminated by Sponsor;
- Participant is determined to be not eligible for Year 1 (Cohort 1 and Cohort 2 participants) or Year 2 IP administration (only for Cohort 2 participants).

- Participants randomized before the approval of protocol amendment 6, but not dosed, will be withdrawn from the study if they meet exclusion criterion 15, based on the retrospective review of the results of the genetic testing by the investigator.

If a request is made to withdraw from the study, an alternative to withdrawal should be offered that would enable the collection of key data, including adverse events. Alternative methods may include phone contact with the participant and/or caregiver. Documentation should be made that all alternatives have been offered to the participant and/or caregiver.

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted. See the SoA for assessments to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

The Early Discontinuation Visit applies only to participants who are enrolled/randomized and then are prematurely withdrawn from the study, except participants withdrawn because they do not fulfil eligibility criteria for Year 1 (Section 6.1.1) or Year 2 administration (only Cohort 2 participants) (Section 7.1). Participants should be queried regarding their reason for withdrawal. The participant will be permanently discontinued both from the study intervention and from the study at that time. Lack of completion of all or any of the withdrawal/early termination procedures will not be viewed as protocol deviations so long as the participant's safety was preserved.

If a participant withdraws from the study, he may request destruction of any remaining samples, taken and not tested, and the Investigator must document any such requests in the site study records and notify the Sponsor accordingly.

If the participant withdraws from the study and also withdraws consent (see Section 7.2.1) for disclosure of future information, no further evaluations should be performed and no additional data should be collected. The Sponsor may retain and continue to use any data collected before such withdrawal of consent.

Lack of completion of all or any of the withdrawal/early termination procedures will not be viewed as protocol deviations so long as the participant's safety was preserved.

7.2.1. Withdrawal of Consent

Participants/caregivers who decline Year 1 IP administration will be withdrawn from the study; those who decline Year 2 IP administration will remain in the study and will continue to be followed as indicated in Section 1.3.1, footnote "f" and in Section 1.3.2, footnotes "bb" and "cc", see also Section 6.5.1, 6.5.2 and 8.2.10. The only exception to this is when a participant/caregiver specifically withdraws consent for any further contact with them or persons previously authorized by the participant to provide this information. Participants or caregiver(s), should notify the Investigator in writing of the decision to withdraw consent from future follow-up, whenever possible. The withdrawal of consent should be explained in detail in the medical records by the Investigator and entered on the appropriate CRF page. In the event that vital status (whether the participant is alive or dead) is being measured,

publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.

7.3. Lost to Follow-Up

A participant will be considered lost to follow up if he repeatedly fails to return for scheduled visits and is unable to be contacted by the site.

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether or not the participant wishes to and/or should continue in the study;
- Before a participant is deemed lost to follow-up, the Investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record;
- Should the participant continue to be unreachable, he will be considered to have withdrawn from the study.
- Discontinuation of specific sites or of the study as a whole is handled as part of Appendix 1.

8. STUDY ASSESSMENTS AND PROCEDURES

The Investigator (or an appropriate delegate at the Investigator site) must obtain a signed and dated ICD and assent, as appropriate, before performing any study specific procedures.

Study procedures and their timing are summarized in the SoA. Protocol waivers or exemptions are not allowed.

Immediate safety concerns should be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The Investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Every effort should be made to ensure that protocol required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside the control of the Investigator that may make it unfeasible to perform the test. In these cases, the Investigator must take all steps necessary to ensure the safety and well-being of the participant. When a protocol required test cannot be performed, the Investigator will document the reason for the missed test and any corrective and preventive actions that he or she has taken to ensure that required processes are adhered to as soon as possible. The study team must be informed of these incidents in a timely manner.

For samples being collected and shipped, detailed collection, processing, storage, and shipment instructions and contact information will be provided to the Investigator site prior to initiation of the study.

The total blood sampling volume for individual participants in this study is approximately 400 mL. The actual collection times of blood sampling may change. Additional blood samples may be taken for safety assessments at times specified by Pfizer, provided the total volume taken does not exceed 5% of the participant's estimated total blood volume during any period of 4 consecutive weeks.

Due to the potential for insufficient blood to be collected in participants with difficult venous access, and to ensure priority samples are collected, the suggested order of sample collection is described below.

NAb to AAV9 (at Screening Visit [Visit 1] and Baseline Visit [Visit 2] only; otherwise drawn after ELISpot). On Day 360 Visit (Visit 20), blood samples for NAb to AAV9 should be collected first, unless collection of clinical safety samples is required for the management of a safety issue.

Clinical safety

ELISpot

ADA

Banked biospecimens for biomarkers

If a participant has a peripherally inserted central catheter (PICC) line, it must only be used for blood collections and not for IP administration.

8.1. Efficacy Assessments

8.1.1. North Star Ambulatory Assessment (NSAA)

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].[60] 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. For two of the 17 items (rise from floor and run/walk 10 meters) the time to complete the skill (in seconds) is also recorded. If the participant is not able to perform the NSAA due to acute illness or injury, and not due to disease progression, the NSAA should be recorded as not done. If, in the opinion of the Investigator, the acute illness or injury has resolved and the participant is still not able to perform the NSAA or has lost ambulation (Section 8.1.6), then this should be reflected in scoring of the NSAA.

In order to assure the ongoing quality of the clinical evaluators' ability to perform functional assessments (NSAA, ankle range of motion and FVC) video recording may be used at pre-specified visits, as indicated in the SoA. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Videos will be reviewed by the master physiotherapist to provide feedback to the clinical evaluators on the method used to perform the functional assessment. Videos will not be used to provide scoring of the participant's functional assessment. The videos will be stored at the site and retained per the record retention requirements until the end of the study.

Whenever possible the same CE should administer the NSAA for the same participant throughout the study.

Additional details regarding the administration and scoring of the NSAA are provided in the Functional Assessment Manual.

8.1.2. Ankle Range of Motion (ROM)

Ankle (talocrural) passive dorsiflexion will be evaluated using goniometry. The development of ankle contractures is common in the age range of the participants, contributes to difficulties with ambulation, and causes pain. The degrees of motion will be recorded. Additional details are provided in the Functional Assessment Manual.

8.1.3. Muscle Biopsies

In order to evaluate the expression and distribution of mini-dystrophin, muscle biopsies will be collected in approximately the first 15 participants randomized into Cohorts 1 and 2 (and their siblings) from sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, with the potential to collect a maximum of 33 if needed. In addition, these samples may be used for the evaluation of exploratory biomarkers that may include markers related to dystrophin, DMD or similar diseases, or the mechanism of action of fordadistrogene movaparvovec.

Open muscle biopsies will be taken from the biceps brachii at two time points, one at Baseline and two post-Baseline. The post-Baseline muscle biopsies will be performed on Day 360 (Visit 19) and on Day 1830 (Visit 41).

The biopsies will be performed by a healthcare professional with adequate experience, as evaluated by the Sponsor beforehand. This procedure will be performed using anesthesia (eg, regional block or under general anesthesia) according to institutional standards, by a qualified anesthesiologist with adequate experience in treating pediatric patients with DMD, as evaluated by the Sponsor beforehand. Muscle biopsies should only be performed after any imaging and functional assessments scheduled for the same visit have been completed. Specific instructions regarding post-operative care will also be provided to the participants and their caregiver(s) after the procedure.

Muscle biopsies will be analyzed centrally and in a blinded fashion. Detailed collection, processing, storage, and shipment instructions will be provided in the biopsy and central laboratory manuals. Additional training on the aforementioned procedures will be provided by the Sponsor or Sponsor representative.

If, following initial processing for the percent normal mini-dystrophin expression using the LC-MS assay and for the percent of muscle fibers expressing mini-dystrophin using the immunofluorescence assay, there is remaining muscle tissue from the biopsy, it may be stored for further analysis. This would enable repeat processing and analysis for these two secondary endpoints, if needed.

In addition, unless prohibited by local regulations or IRB/EC decision, participants will be asked to indicate on the consent document whether they will allow their biopsy samples to be banked so that they might also be used to design and conduct research in order to gain a further understanding of other diseases and to advance science, including development of other medicines for patients. This component of the sampling banking is optional for participants; they may still participate in the study even if they do not agree to the additional research on their banked samples. The optional additional research does not require the collection of any further samples.

In the event of an SAE affecting skeletal and/or cardiac muscle, an ad-hoc muscle biopsy will be performed, if possible, to aid the diagnosis and/or management of the event. If a site has not been previously trained and certified to collect muscle biopsies by the Sponsor or designee, training will be completed before the biopsy is performed. Ad-hoc muscle biopsies will also be analyzed centrally and in a blinded fashion, unless determined otherwise by the investigator or the Sponsor.

Investigators should discuss the possibility of an ad-hoc muscle biopsy with participants and caregivers during the review of the ICD.

8.1.4. Forced Vital Capacity (FVC)

For participants ≥6 years old at the Screening Visit (Visit 1), 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].[63] 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 [Qanjer et al., 2012].[64]

Whenever possible the same CE or trained respiratory therapist (if approved by the sponsor) should perform the spirometry for the same participant throughout the study.

Additional details regarding the assessment of FVC are provided in the Functional Assessment Manual.

8.1.5. Actigraphy

Activity monitors will be placed on the ambulatory participant's ankle prior to performing the NSAA at study visits and are to be worn continuously for the next 2 weeks to capture real-life activities.

8.1.6. Ambulatory Status/Loss of Ambulation

After the Screening Visit (Visit 1) ambulatory status will be assessed as follows:

- At each visit in which an assessment of ambulatory status occurs, per the SoA, the following assessments will occur: caregivers will be asked to report whether the participant is able to walk to perform activities of daily living and, if not, when the last date was on which he was able to do so;
- At each visit when ambulatory status is assessed, the NSAA will be attempted.

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 (LASA) described in the QoL & ADL Manual), AND
- Inability to perform the walk item of 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.

If loss of ambulation occurs, the NSAA will no longer be assessed and the scores will be recorded in the CRF at each visit per SoA, to reflect that the participant was unable to achieve any skill unassisted. Additionally, the ankle activity monitoring will be removed.

8.1.7. Clinical Outcome Assessments

Clinical outcomes assessments (COAs) will be completed by the caregiver and clinical evaluator throughout the study. Ideally, the same caregiver will complete caregiver reported COAs during the study. The same clinical evaluator will administer the NSAA and complete the clinical evaluator reported NSAA anchor question at each visit. Depending on the participant's age, and at the discretion of the Investigator and caregiver, COAs may also be completed by the participants themselves. Details regarding administration of these assessments, training, and any additional requirements will be provided in the Health-Related Quality of Life and Activities of Daily Living Assessment Manual.

8.1.7.1. Caregiver-Completed Assessments

8.1.7.1.1. Modified Pediatric Outcomes Data Collection Instrument (PODCI) – Pediatric Parent

In order to evaluate participants' musculoskeletal health status, PODCI questionnaire scales will be collected. The Modified PODCI – Pediatric Parent includes the Transfer and Basic Mobility Core Scale (11 items) and the Sports and Physical Functioning Core Scale (21 items) from the original PODCI measure for a total of 32 items that assess a participant's ability to walk, stand, and perform activities of daily living. The pediatric parent version will be completed by caregivers of participants. The scales each produce an independent, standardized score ranging from 0-100, with lower scores representing lower levels of function.

8.1.7.1.2. EuroQol 5 Dimensions – Youth Health Questionnaire Proxy Version (EQ-5D-Y Proxy)

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. The EQ-5D-Y Proxy also includes a standard vertical 20 cm visual analogue scale (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. All items refer to the health state "today".

8.1.7.1.3. Patient Global Impression of Severity – Ambulatory Activities of Daily Living (Caregiver-report; PGIS:CG)

The Patient Global Impression of Severity – Ambulatory Activities of Daily Living (Caregiver -report; PGIS:CG) is a caregiver-completed, 2-item measure of their child's current ability to perform daily activities that require the use of their legs (ie, ambulatory motor function). Motor function is assessed using a 5-point Likert scale with the following options: able to do all, able to do many, able to do some, able to do very little, not able to do any. The PGIS:CG is collected to enable an anchor based method for interpreting changes in the NSAA total score and Modified PODCI scale scores. Details of these analyses will be described in a separate analysis plan.

8.1.7.1.4. EQ-5D-5L

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. 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.

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. All items refer to the caregiver's health state "today".

8.1.7.2. Participant Completed Assessments

8.1.7.2.1. Modified PODCI – Adolescent

The Modified PODCI – Adolescent contains a total of 29 items that assess a participant's ability to walk, stand, and perform activities of daily living. Two subscales from the original PODCI are included: the Transfer and Basic Mobility Core Scale (11 items) and the Sports and Physical Functioning Core Scale (18 items). Participants will become eligible to complete the measure at 11 years of age. See Section 8.1.7.1.1.

8.1.7.2.2. EuroQol 5 Dimensions – Youth Health Questionnaire (EQ-5D-Y)

Participants will become eligible to complete the self-report version of the EQ-5D-Y at 8 years of age. See Section 8.1.7.1.2.

8.1.7.2.3. Patient Global Impression of Severity – Ambulatory Activities of Daily Living (Self-report; PGIS)

The Patient Global Impression of Severity – Ambulatory Activities of Daily Living (PGIS) is a self-reported, 2-item measure of a participant's current ability to perform daily activities

that require the use of their legs (ie, ambulatory motor function) adapted from the PGIS:CG (See Section 8.1.7.1.3). Participants will become eligible to complete the PGIS at 11 years of age. The PGIS is collected to enable an anchor-based method for interpreting changes in the NSAA total score and Modified PODCI scale scores. Details of these analyses will be described in a separate analysis plan.

8.1.7.3. Clinical Evaluator-Completed Assessment

8.1.7.3.1. Clinician Global Impression of Severity – Ambulatory Motor Function (CGIS)

The Clinician Global Impression of Severity – Ambulatory Motor Function (CGIS) is a clinical evaluator-reported, 1-item measure of a participant's overall ambulatory motor function. Motor function is assessed using a 5-point Likert scale with the following options: no ambulatory motor function, a little ambulatory motor function, some ambulatory motor function, much ambulatory motor function, complete ambulatory motor function. The recall period is "today". The CGIS will be completed by the same clinical evaluator who completes the NSAA at each visit. The CGIS is collected to enable an anchor-based method for interpreting changes in the NSAA total score and Modified PODCI scale scores. Details of these analyses will be described in a separate analysis plan.

8.1.8. Rater Qualifications

For specific rating assessments, only qualified raters will be allowed to evaluate and/or rate participants in this study. The minimum qualifications a rater must meet for each study rating assessment will be outlined in the Functional Assessment Manual provided to each participating site. The level of experience with the target population (or equivalent), specific scale experience (or equivalent), and certification required (if applicable) will be listed and used to determine whether a rater is approved for a given assessment. Proposed raters who do not meet specific criteria but who may be qualified based on unique circumstances may be individually reviewed by the study clinical team to determine whether or not a waiver may be issued. The rater must become certified to perform selected study assessments before he or she can participate in the conduct of the study. For specifically defined assessments, rater training and standardization exercises may be conducted, and written and signed documentation will be provided by the site for each rater's certification. In return, each site will be provided written and signed documentation outlining each rater's certification for specific study assessments. Recertification may be required at periodic intervals during the study. The raters who administer specific study assessments will be documented in a centralized location and all site staff who administer ratings will be verified in the site study documentation during the conduct of the study. Following certification, a Rater ID will be provided to each CE. The CE is responsible for recording their Rater ID on each completed worksheet.

8.2. Safety Assessments

Planned time points for all safety assessments are provided in the SoA. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety concerns.

8.2.1. Physical Examinations

A complete physical examination will be conducted by a qualified healthcare professional and will include, at a minimum, assessments of the head, ears, eyes, nose, mouth, skin, heart and lung, lymph nodes, gastrointestinal, and musculoskeletal systems.

A brief physical examination will be conducted by a qualified healthcare professional and will include, at a minimum, assessments of general appearance, chest (heart and lungs), abdomen, musculoskeletal (joints, tenderness, presence of new fractures, joint contractures).

Investigators should pay special attention to clinical signs related to previous serious illnesses.

8.2.2. Neurological Examinations

The complete neurological examination will be conducted by a neurologist and will include an assessment of mental status, cranial nerves II-XII, the motor system (upper and lower limb bulk strength, right and left separately), deep tendon reflexes, the sensory system, station, gait, and coordination.

The brief neurological examination will also be conducted by a neurologist and will include an assessment of the motor system (upper and lower limb bulk strength, right and left separately) as well as station and gait.

8.2.3. Height and Weight Measurements

Weight will be measured with a calibrated digital scale placed on a stable, flat surface. Sites may use a sponsor-provided calibrated scale or their own institutional calibrated scale. Body weight measurement must be verified by two site personnel. Participants must remove shoes, bulky layers of clothing, and jackets so that only light clothing remains. They must also remove the contents of their pockets and remain still during measurement of weight. Preferably both height and weight measurements will be collected in the morning. Participants should be instructed to step gently onto the scale, place both feet together in the center of the scale and stand straight with eyes directed ahead. Participants should be instructed to stand still and not sway. Measurement will be recorded after the weight has stabilized. Body weight should be reported with precision to one decimal place (eg, 0.1 kg).

A 10-kg certified weight will be purchased by the Sponsor and sent to each site. To assess the accuracy of the scale, the trial coordinator or appointed designee will weigh him or herself alone, then the weight alone, and finally, the individual together with the weight. Deviations of more than one scale division (±0.1 kg) will require corrective action and the Sponsor must be contacted. Accuracy checks will be performed before each visit when weight is to be measured. For participants who are no longer able to stand, weight will be measured, if possible, using a wheelchair scale.

Height will be measured with the participant standing without shoes on a flat surface and with the heels touching the ground. For participants who are not able to stand, or who have

contractures that prevent standing with the heels on the ground, height will not be measured but will be estimated by ulna length. Refer to the Functional Assessment Manual for details.

8.2.4. Vital Signs

Body temperature, pulse rate, respiratory rate, and supine blood pressure will be assessed before blood collection for laboratory tests.

Supine blood pressure and pulse rate measurements will be assessed once with a completely automated device. Manual techniques will be used only if an automated device is not available.

Blood pressure and pulse rate measurements should be preceded by at least 5 minutes of rest for the participant in a quiet setting without distractions (eg, television, cell phones).

O2 saturation will only be measured before the start of the IP infusion and during the inpatient stay post IP administration (see Sections 1.3.1 and Section 1.3.2).

8.2.5. Electrocardiograms

A single 12-Lead ECG will be collected using an ECG machine, provided by the Sponsor, that automatically calculates the heart rate and measures PR, QT, corrected QT (QTc) intervals and QRS complex. The Fridericia corrected QTc (QTcF) will be the basis for safety monitoring of QT intervals. All scheduled ECGs should be performed after the participant has rested quietly for at least 10 minutes in the supine position. ECG data will be submitted to a central laboratory for measurement and interpretation and will also be reviewed at the site for safety monitoring.

If a post-dose QTcF interval remains ≥30 msec from the baseline **and** is >450 msec; or b) an uncorrected QT or QTcF value is ≥500 msec for any scheduled ECG for greater than 4 hours (or sooner, at the discretion of the Investigator), or if QTcF intervals get progressively longer, the participant should undergo continuous ECG monitoring. A cardiologist should be consulted if QTc intervals do not return to less than the criteria listed above after 8 hours of monitoring (or sooner, at the discretion of the Investigator).

The final ECG report from the central laboratory should be maintained in the participant's source documentation as well as the final interpretation of the ECG recording. Any clinically significant changes from the Screening ECG may potentially be AEs (Appendix 7) and should be evaluated further, as clinically warranted.

If the leads are placed incorrectly on the participant´s limbs, the ECG should be repeated. It is important that leads be placed in the same and correct positions each time in order to achieve precise ECG recordings. If a machine-read QTc value is prolonged, the Fridericia QT correction should be obtained to interpret whether a safety event has occurred as defined above.

ECG values of potential clinical concern are listed in Appendix 7.

8.2.6. Echocardiogram

Echocardiograms will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

To ensure safety of the participants, a qualified individual at the site will evaluate the echocardiogram at least for left ventricular ejection fraction (LVEF), but other parameters may also be assessed, including but not limited to myocardial strain. Echocardiogram should be performed using a 2-D imaging collection method.

If the LVEF is below 50% on the echocardiogram at any visit after screening, the participant should be referred to a cardiologist for further assessment.

8.2.7. Cardiac Troponin I

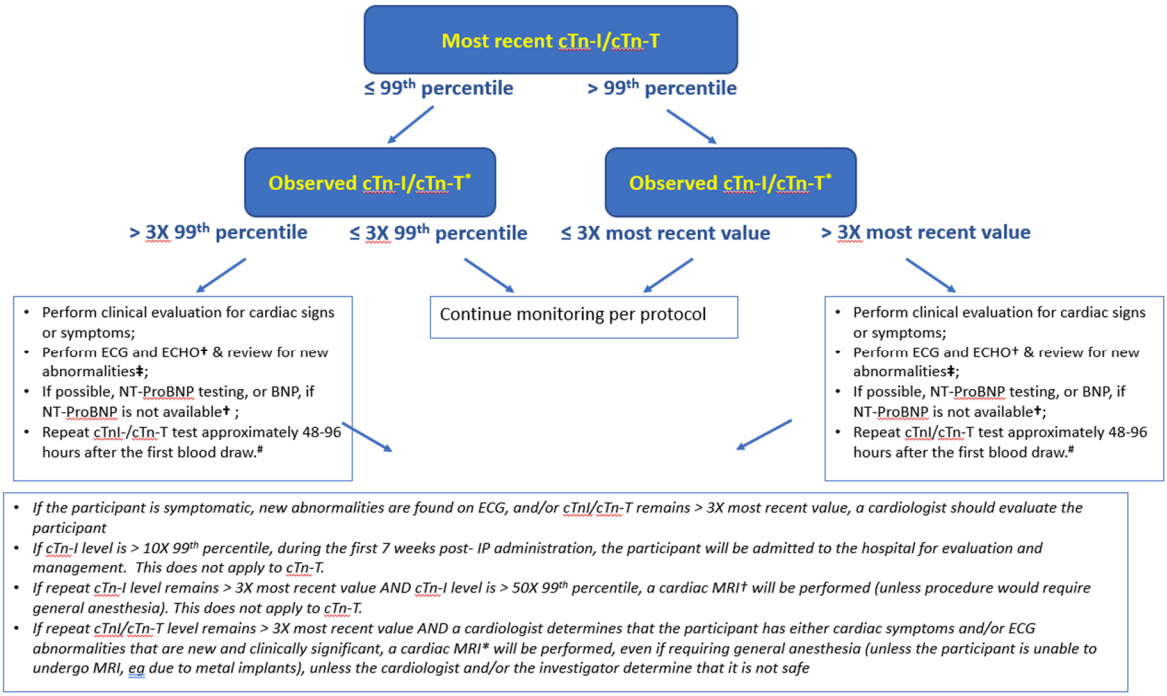
To monitor for cardiac injury, cTn-I will be assessed. If a local laboratory cannot perform the cTn-I assay, cTn-T can be substituted for the local laboratory assessments.

If a participant presents with a Screening cTn-I value >3 x 99th percentile the following instructions should be followed:

- Perform clinical evaluation for cardiac signs or symptoms;
- Review Screening ECG for significant findings suggestive of ischemia;
- If either of the above is positive, repeat cTn-I approximately 48 to 96 hours after the first blood draw and request a cardiology consult.

The algorithm in Figure 3 provides instructions for the management of elevated cTn-I (or cTn-T) values during the course of the study, after the Screening visit.

Figure 3. Management of Elevated Cardiac Troponin I (cTn-I)/Cardiac Troponin T (cTn-T) values



*Results of cTn-I should only be compared to results of cTn-I and results of cTn-T should only be compared to results of cTn-T.
†Echocardiogram and NT-ProBNP/BNP are required only during the first 14 days post IP administration.
‡ECG, echocardiogram, and cardiac MRI (original and follow-up scans) performed during the evaluation of an elevated cardiac troponin value must be read locally for immediate interpretation and safety monitoring and will be submitted to a central reader as soon as possible (i.e., in less than 72 hours) for standardized interpretation. For events of elevated troponin or myocarditis with or without abnormal findings in the initial cardiac MRI, a follow up cardiac MRI will be performed approximately 3 months after the start of the event. This cardiac MRI will be reviewed at the site for safety monitoring and will also be submitted to the imaging CRO for measurement and interpretation as soon as possible (i.e., in less than 72 hours).
Sites will repeat troponin and NT-ProBNP tests (or BNP, if NT-ProBNP is not available) approximately every 48-72 hours until each test returns to Baseline values or reaches a level considered not clinically significant by the investigator.

NOTE: If at any time during the study a participant presents with a cTn-I value >3 x 99th percentile and he had not been previously evaluated, the instructions for evaluation outlined in the algorithm should be followed.

8.2.8. Cardiac MRI

Cardiac MRI will be performed using a 1.5T or 3.0T scanner with an appropriate coil for cardiac imaging. The scan may include imaging before and after IV administration of a gadolinium-based contrast agent. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration. If the site

considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed.

Complete details on the cardiac MRI acquisition protocol, image quality review, and transmission of data to the imaging contract research organization (CRO) will be provided in an Imaging Manual offered to the study sites. The imaging CRO will include central review of all cardiac MRI scans. The central reviewer analysis will include, at a minimum, evaluation of LVEF, myocardial fibrosis as measured by late gadolinium enhancement (LGE) if gadolinium is used, and evaluation of myocardial strain. Cardiac MRIs (original and any follow-up scans) performed due to an acute event, as per Section 8.2.7, will be submitted to the imaging CRO for measurement and interpretation as soon as possible (i.e., in less than 72 hours), and will also be reviewed at the site for safety monitoring. For events of elevated troponin or myocarditis with or without abnormal findings in the initial cardiac MRI, a follow up cardiac MRI will be performed approximately 3 months after the start of the event. This cardiac MRI will be reviewed at the site for safety monitoring and will also be submitted to the imaging CRO for measurement and interpretation as soon as possible (i.e., in less than 72 hours).

8.2.8.1. Management of Incidental Findings

An incidental finding is one unknown to the participant that has potential health or reproductive importance, which is discovered unexpectedly in the course of a research study, but is unrelated to the purpose and beyond the aims of the study.

Cardiac MRI images will be reviewed by the central review facility. The purpose of this review is to evaluate images for LVEF, LGE, and strain over time. Central image review is not a complete medical review of the participant. If, during the central review process, an unexpected observation is identified and this finding could, in the opinion of the central reviewer, have a significant health or reproductive consequence, this finding may be shared with the study sponsor for disclosure to the investigator. All follow-up testing and final diagnosis will be left to the discretion of the medical professionals at the site or those with an existing physician participant relationship. The investigator will be responsible for reporting any AEs identified from incidental findings as described in the AE reporting section. Identification of such incidental findings during the central review process should not be expected, and the site maintains responsibility for performing a general safety review of all images in accordance with site protocols.

8.2.9. Clinical Safety Laboratory Assessments

See Appendix 2 for the list of clinical safety laboratory tests to be performed and the SoA for the timing and frequency.

The Investigator or their designee must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF. Clinically significant abnormal laboratory findings are those which are not associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the participant's condition.

All laboratory tests with values considered clinically significantly abnormal during participation in the study should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the Investigator or medical monitor.

If such values do not return to normal/baseline within a period of time judged reasonable by the Investigator, the etiology should be identified and the Sponsor notified.

All protocol-required laboratory assessments, as defined in Appendix 2, must be conducted in accordance with the laboratory manual and the SoA.

8.2.10. Post IP Intensified Safety Monitoring (at Year 1 and Year 2)

Due to the potential for an immune reaction against the AAV9 vector and/or the transgene, participants will undergo an intensified safety monitoring period for the first 34 days after IP administration in Year 1 and in Year 2.

Following IP administration, participants will be monitored as inpatients for 7 days, or longer, if deemed necessary by the Investigator (see SoA for details). Participants must be in an individual room, ie, not shared with other patients. Following IP administration, it is recommended that the IV line remains for at least 48 hours in case IV hydration or treatment is necessary due to nausea, vomiting, anorexia, etc. Once the IV line is removed, volume status should be assessed regularly, and if a participant subsequently experiences nausea or vomiting, consideration should be given to the placement of an IV line for treatment with an IV anti-emetic, hydration and replacement of the oral protocol-mandated glucocorticoid regimen by an IV regimen (see Section 6.5.1). Upon discharge, participants will be asked to stay local to the site (ie, if they do not live near the site, they will be asked to stay in at an overnight facility) through Day 14 after Year 1 and Year 2 IP administration, or longer, if deemed necessary by the Investigator. If adverse events possibly related to IP administration are observed, participants should not be discharged until the events have resolved.

Once enrollment is complete and the last participant has completed 14 days post Year 1 IP administration, the E-DMC will review the safety information accrued to determine if any changes to the Year 2 IP administration schedule, including need for and length of hospitalization, are required.

During the first 34 days post IP administration participants will undergo study visits on:

- Year 1: Day 2 (Visit 4), Day 4 (Visit 5), Days 6-10 (Visits 6-10), Day 14 (Visit 11), Day 21 (Visit 12, a remote visit is allowed) and Day 34 (Visit 13), for clinical and laboratory assessments.

- Year 2: Day 2 (Visit 21), Day 4 (Visit 22), Days 6-10 (Visits 23-27), Day 14 (Visit 28), Day 21 (Visit 29, a remote visit is allowed) and Day 34 (Visit 30), for clinical and laboratory assessments. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend these visits (see Section 1.3.2 footnote "bb", and Appendix 12).

Local Laboratory Assessments

- On Visit 2 and Visits 4 to 10 (Day 2 to 10) at Year 1, and Visits 20 to 27 (Days 1 to 10) at Year 2, the sites will perform blood and urine safety tests at their local laboratories. This will ensure a very rapid turnaround (within 1 to 2 hours) and review of the results during a period that is critical for the detection of immune mediated-adverse events.

- When copies of medical records including local laboratory reports are provided to Pfizer for the purpose of critical safety review, all participant identifiers, with the exception of the participant number, must be redacted on the copies of the medical records before submission to Pfizer. The files should be password-protected.

Participants and their caregivers will be instructed to carefully monitor the liquid intake and urinary output of the participants for the first 34 days post IP administration (see Section 5.5.2 for additional details). Participants will be required to return to the site for evaluation by the Investigator or designated medically qualified individual, within 24 hours if any of the following occur:

- No urine output for 12 hours, or a significant change in urine output in less than 24 hours, or observation of tea-colored urine;

- Evidence of significant reduction in estimated glomerular filtration rate, determined by clinically relevant increases in serum cystatin C or serum creatinine (eg, doubling) from value at the Screening Visit (central laboratory) or from value at the Baseline Visit (local laboratory) at Year 1 or from Visit 19 at Year 2;

- Clinically relevant increase from Screening value in hematocrit or hemoglobin;

- Presence of anion gap acidosis;

- Abnormality on blood smear, or haptoglobin <LLN or reduced to <50% from Screening value (indicating unequivocal hemolysis);

- Platelets <75 x 10^3/µl.

Hospital admission and/or treatment with eculizumab, as per Section 6.5.1, or additional immunosuppression may be warranted, at the discretion of the Investigator and/or Sponsor.

Since admission to the intensive care or coronary unit is a possibility which could involve placement of a central catheter and/or an endomyocardial biopsy to aid diagnosis and management, and/or mechanical circulatory and/or respiratory support, investigators should discuss the possibility of these interventions with the pediatric cardiologist (sub-investigator). These measures should be discussed with participants and caregivers during the review of the ICD.

Investigators in Japan should see Section 10.10 (Appendix 10) for details on the management of the participants during the first 14 days post IP administration.

8.2.11. Additional Safety Monitoring

Caregivers should be instructed to monitor participants, particularly within the first 90 days following each IP administration, to determine if they have a significant change in their ability to perform typical activities of daily living including chewing, swallowing, speaking, and walking, or if they have cardiac symptoms such as chest pain or pressure, palpitations, shortness of breath, edema in the lower extremities, or dizziness. If any of these occur, participants (and/or caregivers) should be instructed to promptly contact the site for a possible unscheduled visit and/or biospecimen collection. Investigators will closely monitor the participant during this time for muscle weakness or any other signs or symptoms of skeletal or cardiac muscle inflammation or injury. All DMD participants permitted in the study, including those with mutations between exons 30-41 or at exon 55, may be at potential risk of heart muscle injury and/or skeletal muscle damage or inflammation and will be carefully monitored as indicated above.

8.2.12. Local and Central Laboratory Testing

Some of the laboratory testing at Year 1 and at Year 2 will be made by the local laboratory at each site to ensure fast turnaround of test results. In order to preserve the blinding of the study by no sharing the results of sensitive clinical data (Section 6.3.3), **on some of these visits the sites will also send a separate sample to the central laboratory** for C3 and C4 analysis. For the same reason, AST and ALT will not be analyzed locally and instead, to monitor hepatic safety, at Year 1, on Day 9 (Visit 9) and at Year 2 on Day 9 (Visit 26), the sites will send a separate sample to the central laboratory for GLDH analysis. Cardiac troponin will also be analyzed by the central laboratory at Day 7 (Visit 7) in Year 1 and Day 7 (Visit 24) in Year 2. Cardiac troponin I (or cardiac troponin T when cardiac troponin I is not available) will be assessed locally at the following visits: Baseline Visit (Visit 2), Day 2 (Visit 4), Day 4 (Visit 5), Day 6, Day 8, and Day 10 (Visit 6, Visit 8, and Visit 10) in Year 1; Day 390 (Visit 20) pre-IP administration, Day 391 (Visit 21), Day 393 (Visit 22), Day 395 (Visit 23), Day 397 (Visit 25) and Day 399 (Visit 27) in Year 2. Local serum creatinine will also be collected at the following visits: Baseline Visit (Visit 2), Day 2 (Visit 4) and Day 4 (Visit 5) in Year 1, and Day 390 (Visit 20) pre-IP administration, Day 391 (Visit 21) and Day 393 (Visit 22) in Year 2. See Appendix 2 for additional details. For sites in Japan only: local and central laboratory testing will also be collected at Visits 4 and 5 in Year 1, and Visits 21 and 22 in Year 2; see Appendix 2 for details. For sites in Russia, local and central laboratory testing will also be collected from Day 14 (Visit 11) to Day 240 (Visit 17) in Year 1, and from Day 403 (Visit 28) to Day 629 (Visit 34) in Year 2; see Appendix 2 and Appendix 15 for details.

Table 2. Routine Local Laboratory Testing in Year 1 and Year 2

Year 1 Visits	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8&9	Visit 10
Year 2 Visits	N/A	N/A	Visit 20	Visit 21	Visit 22	Visit 23	Visit 24	Visits 25&26	Visit 27
Hematology				X[a]	X[a]	X	X	X	X
Chemistry and hepatic safety				X[a]	X[a]	X	X	X	X
Cystatin C[c]				X[a]	X[a]	X[c]	X[c]	X[c]	X[c]
Urinalysis				X[a]	X[a]	X	X	X	X
Cardiac troponin I (or T)		X	X[b]	X	X	X		X[d]	X
Serum creatinine		X	X[b]	X	X				
Haptoglobin				X[a]	X[a]				

a. Only for sites in Japan.

b. To be collected pre-IP administration, and only at Year 2, Visit 20.

c. To be analyzed when possible at the site.

d. Only at Visit 8 in Year 1, and at Visit 25 in Year 2.

Note that this table only shows the local laboratory tests to be collected at these visits. For complete information, including what laboratory tests are sent to the central laboratory see Appendix 2.

8.2.13. Mood and Behavior Risk Monitoring

The Child Behavior Check List (CBCL) was 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. The caregiver will complete the age-appropriate version of the CBCL at Screening (Visit 1) and subsequent visits, as indicated on the SoA, based on the participant's behavior. 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 for high-risk behaviors. 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 Internalizing global scale indicate clinically significant behaviors.

An assessment of the participant's psychological status will be completed by the Investigator if a participant has a CBCL T-score of ≥65 in the Withdrawn or Withdrawn/Depressed syndrome scales and/or a T-score of ≥60 in the Internalizing global scale. The Investigator is required to determine whether it is safe for the participant to enroll and/or continue study participation and/or if additional assessment is indicated. If additional assessment is indicated, and/or if scores remain elevated on subsequent assessment, and/or if an event of

self-harm occurs, an evaluation will be performed by one of the following child and adolescent mental health providers (MHP):

- In the United States: 1) Child and Adolescent Psychiatrists (board certified or board eligible), or psychiatrists who have training and experience in the diagnosis and treatment of psychiatric disorders in the pediatric population, or 2) Psy. D. or Ph.D. level Clinical Psychologists, licensed Master's level Clinical Social Workers or licensed Psychiatric Nurse Practitioners who have training and experience in the diagnosis and treatment of psychiatric disorders in the pediatric population.

- In countries outside the United States: individuals with similar training and experience as those described above.

Written documentation of the risk assessment by the Investigator and/or the MHP should be included in the participant's source documentation and the risk assessment CRF will be completed. The risk assessment CRF serves as further verification that the psychiatric evaluation and assessment of participant safety have been completed.

If the MHP determines that additional psychiatric assessment is warranted, the participant should be referred to a psychiatrist or psychologist for further assessment.

Additional details regarding these assessments, including training and any additional requirements, will be provided.

8.2.14. Pregnancy Testing

Not applicable.

8.3. Adverse Events and Serious Adverse Events

The definitions of an AE and an SAE can be found in Appendix 3.

AEs will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative).

The Investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible to pursue and obtain adequate information both to determine the outcome and to assess whether it meets the criteria for classification as an SAE or that caused the participant to discontinue the study (see Section 7).

In addition, the Investigator may be requested by Pfizer Safety to obtain specific follow-up information in an expedited fashion.

8.3.1. Time Period and Frequency for Collecting AE and SAE Information

The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant begins from the time the participant provides informed consent,

which is obtained before the participant's participation in the study (ie, before undergoing any study-related procedure and/or receiving investigational product), through and including a minimum of 1 year after the last IP administration.

In the Long-term Follow-up period (ie, Years 3 through 6), active elicitation and collection of AEs and SAEs occurs on a bi-yearly basis.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

Follow-up by the Investigator continues throughout and after the active collection period and until the event or its sequelae resolve or stabilize at a level acceptable to the Investigator, and Pfizer concurs with that assessment.

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant definitively discontinues or temporarily discontinues the study because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported using the CT SAE Report Form.

Investigators are not obligated to actively seek AEs or SAEs after conclusion of the study participation. However, if the Investigator learns of any SAE, including a death, at any time after a participant has been discharged from the study, and he/she considers the event to be reasonably related to the study intervention or study participation, the Investigator must promptly notify the Sponsor.

8.3.1.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period are reported to Pfizer Safety on the CT SAE Report Form immediately and under no circumstance should this exceed 24 hours, as indicated in Appendix 3. The Investigator will submit any updated SAE data to the Sponsor within 24 hours of it being available.

SAEs occurring in a participant after the active collection period has ended are reported to Pfizer Safety if the Investigator becomes aware of them; at a minimum, all SAEs that the Investigator believes have at least a reasonable possibility of being related to investigational product must be reported to Pfizer Safety.

8.3.1.2. Recording Nonserious AEs and SAEs on the CRF

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, will be recorded on the AE section of the CRF.

During the active collection period, both nonserious AEs and SAEs are recorded on the CRF.

8.3.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in Appendix 3.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.3.3. Follow-up of AEs and SAEs

After the initial AE/SAE report, the Investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the Investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

In general, follow-up information will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety.

Further information on follow-up procedures is given in Appendix 3.

8.3.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the Investigator to the Sponsor of an SAE is essential so that legal obligations and ethical responsibilities towards the safety of participants and the safety of a study intervention under clinical investigation are met.

The Sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The Sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, institutional review boards (IRBs)/ethics committees (ECs), and Investigators.

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions (SUSARs) according to local regulatory requirements and Sponsor policy and forwarded to Investigators as necessary.

An Investigator who receives an Investigator safety report describing an SAE or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will review and then file it along with the Investigator's brochure and will notify the IRB/EC, if appropriate according to local requirements. Investigators in Japan should see Section 10.10 (Appendix 10).

8.3.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Environmental exposure occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members, and others who may be exposed. An environmental exposure may include EDP, EDB, and occupational exposure.

Any such exposures to the study intervention under study are reportable to Pfizer Safety within 24 hours of Investigator awareness.

8.3.5.1. Exposure During Pregnancy

An EDP occurs if:

- A male participant who received study intervention inseminates a female partner.
- A female nonparticipant is found to be pregnant while being exposed or having been exposed to study intervention due to environmental exposure. Below are examples of environmental EDP:
    - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by skin, mucosal contact, or ingestion.
    - A male family member or healthcare provider who has been exposed to the study intervention by skin, mucosal contact, or ingestion then inseminates his female partner .
    - A female nonparticipant reports that she is pregnant and has been exposed through viral shedding by a study participant within 2 months after dosing, and a month prior to or during pregnancy.
    - A male nonparticipant who has been exposed through viral shedding by a study participant within 2 months after dosing of study drug inseminates a pregnant female a month prior to or during the pregnancy.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in a participant's partner, the investigator must report this information to Pfizer Safety on the CT SAE Report Form and an EDP Supplemental Form, regardless of whether an SAE has occurred. Details of the pregnancy will be collected after the start of study intervention and until study end.

- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer Safety using the CT SAE Report Form and EDP Supplemental Form. Since the exposure information does not pertain to the participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

Follow up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow up to the initial EDP Supplemental Form. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless preprocedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly [in a live born baby, a terminated fetus, an intrauterine fetal demise, or a neonatal death]), the investigator should follow the procedures for reporting SAEs. Additional information about pregnancy outcomes that are reported to Pfizer Safety as SAEs follows:

- Spontaneous abortion including miscarriage and missed abortion should be reported as an SAE;

- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the study intervention.

Additional information regarding the EDP may be requested by the sponsor. Further follow up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

8.3.5.2. Exposure During Breastfeeding

An EDB if:

- A female nonparticipant is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure). An example of environmental exposure during breastfeeding is a female family member or healthcare

provider who reports that she is breastfeeding after having been exposed to the study intervention by skin, mucosal contact, or ingestion.

- A female nonparticipant is found to be breastfeeding while having been exposed through viral shedding by a study participant within 2 months after dosing of study drug, and a month prior to or during breast feeding.

The investigator must report exposure during breastfeeding to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported using the CT SAE Report Form. When exposure during breastfeeding occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so the information is not recorded on a CRF. However, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

An EDB report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accord with authorized use. However, if the infant experiences an SAE associated with such a drug, the SAE is reported together with the EDB.

8.3.5.3. Occupational Exposure

The investigator must report any instance of occupational exposure to Pfizer Safety within 24 hours of the investigator's awareness using the CT SAE Report Form, regardless of whether there is an associated SAE. Since the information does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

8.3.6. Cardiovascular and Death Events

Collected as part of routine safety monitoring.

8.3.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not applicable.

8.3.8. Adverse Events of Special Interest

Not applicable.

8.3.8.1. Lack of Efficacy

Not applicable.

8.3.9. Medical Device Deficiencies

Not applicable.

8.3.10. Medication Errors

Medication errors may result from the administration or consumption of the investigational product by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Exposures to the investigational product under study may occur in clinical trial settings, such as medication errors.

Safety Event	Recorded on the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
Medication errors	All (regardless of whether associated with an AE)	Only if associated with an SAE

Medication errors include:

- Medication errors involving participant exposure to the investigational product;
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the study participant.

Such medication errors occurring to a study participant are to be captured on the medication error page of the CRF, which is a specific version of the AE page.

In the event of a medication dosing error, the Sponsor should be notified within 24 hours.

Whether or not the medication error is accompanied by an AE, as determined by the Investigator, the medication error is recorded on the medication error page of the CRF and, if applicable, any associated AE(s), serious and nonserious, are recorded on an AE page of the CRF.

Medication errors should be reported to Pfizer Safety within 24 hours on a CT SAE Report Form **only when associated with an SAE.**

8.4. Treatment of Overdose

For this study, any dose of fordadistrogene movaparvovec greater than a single administration of 2E14 vg/kg will be considered an overdose. Sponsor does not recommend specific treatment for an overdose.

In the event of an overdose, the Investigator/treating physician should:

1. Contact the medical monitor within 24 hours.
2. Closely monitor the participant for any AEs/SAEs and laboratory abnormalities for at least 34 calendar days after the overdose of fordadistrogene movaparvovec.

3. Obtain a blood sample for pharmacokinetic (PK) analysis within [x] days from the date of the last dose of study intervention if requested by the medical monitor (determined on a case by case basis). Vector shedding will be assessed as a surrogate for PK. In Year 1 the assessment of vector shedding in whole blood is already planned for Day 2 (Visit 4), Day 4 (Visit 5), and Day 10 (Visit 10), and in the event of an overdose, additional assessments will be added on Day 1 (Visit 3) and Day 14 (Visit 11). The assessment of vector shedding in saliva and urine will be done as planned. In Year 2, the same sampling schedule (whole blood, saliva and urine) for an overdose as in Year 1 will be followed. Both at Year 1 and Year 2, the sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

4. Document the quantity of the excess dose as well as the duration of the overdose in the CRF.

5. Overdose is reportable to Safety **only when associated with an SAE**.

Decisions regarding dose interruptions or modifications will be made by the Investigator in consultation with the medical monitor based on the clinical evaluation of the participant.

8.5. Pharmacokinetics

Pharmacokinetic parameters are not evaluated in this study.

8.6. Pharmacodynamics

Pharmacodynamic parameters are not evaluated in this study.

8.7. Genetics

8.7.1. Specified Genetics

A blood sample for deoxyribonucleic acid (DNA) isolation may be collected. DNA samples will be analyzed for the purpose of confirming the diagnosis of DMD at Screening (Visit 1) by the central laboratory, if the Investigator determines that the results of the prior genetic test are inconclusive.

Details on processes for collection and shipment of these samples can be found in Laboratory Manual.

8.7.2. Banked Biospecimens for Genetics

A 2-mL whole blood sample optimized for DNA isolation Prep D1.5 will be collected as local regulations and IRBs/ECs allow, if limits on blood volume collection have not been exceeded.

Banked biospecimens may be used for research related to drug response and DMD. Genes and other analytes (eg, proteins, RNA, non-drug metabolites) may be studied using the banked samples.

Unless prohibited by local regulations or IRB/EC decision, participants will be asked to indicate on the consent document whether they will allow their banked biospecimens to also be used to design and conduct research in order to gain a further understanding of other diseases and to advance science, including development of other medicines for patients. This component of the sampling banking is optional for participants; they may still participate in the study even if they do not agree to the additional research on their banked biospecimens. The optional additional research does not require the collection of any further samples.

See Appendix 5 for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in Laboratory Manual.

8.8. Biomarkers

Collection of samples for biomarkers research is also part of this study.

8.8.1. Specified Gene Expression (RNA) Research

Specified gene expression (RNA) research is not included in this study.

8.8.2. Specified Protein Research

Specified protein research is not included in this study.

8.8.3. Specified Metabolomic Research

Specified metabolomic research is not included in this study.

8.8.4. Banked Biospecimens for Biomarkers

A 1-mL whole blood (Prep B2.5), 1-mL whole blood (Prep B1.5), and 5-mL urine (Prep M4) samples will be collected as local regulations and IRB/ECs allow, if limits on blood volume collection have not been exceeded.

Banked biospecimens may be used for research related to drug response and DMD. Genes and other analytes (eg, proteins, RNA, nondrug metabolites) may be studied using the banked samples.

Unless prohibited by local regulations or IRB/EC decision, participants will be asked to indicate on the consent document whether they will allow their banked samples to also be used to design and conduct research in order to gain a further understanding of other diseases and to advance science, including development of other medicines for patients. This component of the sampling banking is optional for participants; they may still participate in the study even if they do not agree to the additional research on their banked samples. The optional additional research does not require the collection of any further samples.

See Appendix 5 for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in Laboratory Manual.

8.8.5. Viral Vector Shedding Analysis

Whole blood (1.8 mL), saliva (4.2 mL), and urine (7.2 mL) 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). Potential visits at which samples are to be collected are detailed in the SoA. For each of the approximately first 45 treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. An unblinded qualified Sponsor representative, independent and firewalled from the study team, will review the viral vector shedding results for each participant on an ongoing basis and will communicate with the sites when sampling in a given matrix for each participant should be stopped. The viral vector shedding results will not be shared with the sites. To maintain the study blind, the unblinded qualified Sponsor representative will select Cohort 2 participants (as available) to also have the sampling of the same matrix stopped every time the sampling in a given matrix is stopped for a Cohort 1 participant. An attempt will be made to match these Cohort 2 participants to the specific matrix and timing of Cohort 1 participants.

Detailed collection, processing, storage, and shipment instructions will be provided in the central laboratory manual to maintain sample integrity for each sample type.

The assay reflects the presence of DNA unique to fordadistrogene movaparvovec. Results below the lower limit of quantification (LLOQ) will be reported as below the limit of quantification (BLQ) and will be considered negative. Additionally, saliva and urine samples for all time points from a subset of participants will be analyzed for deoxyribonuclease-resistant particles.

As part of understanding the disease and advance science, samples may be used for further characterization and/or evaluation. These data will be used for internal exploratory purposes and will not be included in the clinical study report. Samples collected for this purpose will be retained in accordance to local regulations and if not used, will be destroyed.

8.8.6. Study C3391007 Household Contact Immunogenicity

To further understand the development of antibodies to AAV9 (ie, seroconversion) due to household contact with a participant treated with fordadistrogene movaparvovec, a study may be performed under a separate protocol. Seroconversion rates from this separate study may be estimated prior to unblinding (either for an interim analysis or the primary analysis) of study C3391003. The integrity of the C3391003 study blind will be maintained by the use of an independent, external team of statistician(s) and programmer(s) to estimate the seroconversion rates. Only summary seroconversion rates will be communicated.

8.9. Health Economics

8.9.1. Healthcare Resource Utilization Questionnaire – Caregiver (HRU:CG)

The Healthcare Resource Use questionnaire is a 4-item, caregiver-completed measure that asks about healthcare resource utilization related to their child's use of healthcare

professionals, emergency room visits, and hospitalizations related to DMD. Caregivers are also asked to estimate out-of-pocket costs related to healthcare resource utilization. The recall period is the past 3 months.

8.9.2. Work Productivity and Activity Impairment DMD Questionnaire – Caregiver (WPAI:DMD Caregiver)

The WPAI:DMD Caregiver is a 6-item, caregiver-completed questionnaire that measures the effect of a child being diagnosed with DMD on caregiver work productivity and impairment. The WPAI:DMD Caregiver yields four scores: absenteeism (work time missed); presenteeism (impairment at work/reduced on the job effectiveness); work productivity loss (overall work impairment/absenteeism plus presenteeism); and activity impairment. Each score is expressed as a percentage (0-100%) with higher numbers indicating greater impairment and less productivity (Reilly et al, 1993).[65] The recall period is the past 7 days.

8.10. Immunogenicity

8.10.1. Neutralizing Antibody to AAV9

Blood samples for analysis of NAb to AAV9 will be collected. Detailed collection, processing, storage, and shipment instructions will be provided in the central laboratory manual.

Samples will be analyzed using validated analytical methods in compliance with Pfizer standard operating procedures (SOP).

As part of understanding of the immunogenicity of the fordadistrogene movaparvovec, samples may be used for further characterization and/or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and will not be included in the clinical report. Samples collected for this purpose will be retained in accordance to local regulations and if not used, will be destroyed.

8.10.2. ELISpot

Blood samples to provide peripheral blood mononuclear cells for analysis of cellular immune responses to mini-dystrophin and AAV9 will be collected.

Detailed collection, processing, storage, and shipment instructions are provided in the central laboratory manual.

As part of understanding of the immunogenicity of fordadistrogene movaparvovec, samples may be used for further characterization and/or evaluation of the bioanalytical method. In addition, residual of these samples may be used for the evaluation of exploratory biomarkers of immune response. These data will be used for internal exploratory purposes and will not be included in the clinical report. Samples collected for this purpose will be retained in accordance to local regulations and if not used, will be destroyed.

8.10.3. Anti-drug Antibodies

Blood samples for analysis of anti-transgene (mini-dystrophin) and anti-AAV9 antibodies will be collected. However, these will only be tested if clinically indicated (eg, clinical immune response to fordadistrogene movaparvovec).

Detailed collection, processing, storage, and shipment instructions will be provided in the central laboratory manual.

Samples will be analyzed using validated analytical methods in compliance with Pfizer standard operating procedures.

As part of understanding of the immunogenicity of the fordadistrogene movaparvovec, samples may be used for further characterization and/or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and will not be included in the clinical report. Samples collected for this purpose will be retained in accordance to local regulations and if not used, will be destroyed.

9. STATISTICAL CONSIDERATIONS

Detailed methodology for summary and statistical analyses of the data collected in this study is outlined here and further detailed in a statistical analysis plan (SAP), which will be maintained by the Sponsor. The SAP may modify what is outlined in the protocol where appropriate; however, any major modifications of the primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

9.1. Estimands and Statistical Hypotheses

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 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.

1. Change from Baseline at Week 52 in the 10 meter run/walk velocity.
2. Change from Baseline at Week 52 in the rise from floor velocity.
3. Number of skills either improved or maintained at Week 52 based on the individual items of the NSAA.
4. 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 I error 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 the Interim Analysis 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 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 MMRM model or the generalized mixed model described in Section 9.4.1.

If either interim analysis is performed, a group sequential approach will be applied to the efficacy analyses to control Type I error 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.

9.1.1. Estimands

Primary Estimand: This estimand will be the primary estimand and will be the difference in mean change from Baseline at Week 52 in the NSAA total score between fordadistrogene movaparvovec and placebo regardless of adherence to background and protocol-mandated glucocorticoid regimens (see Section 6.5.1) during the first 52 weeks:

- 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;
- Death or loss of ambulation are identified as potential intercurrent events. Details on how these intercurrent events are handled in the analysis are provided in the SAP
- Population-level summary: Difference in mean changes from Baseline at Week 52 in the NSAA total score between fordadistrogene movaparvovec and placebo.

9.2. Sample Size Determination

A sufficient number of participants will be screened to achieve a total of approximately 99 participants in the FAS (see Section 9.3). Participants will be randomly assigned in a 2:1 fashion to Cohort 1 (approximately 66 participants) or Cohort 2 (approximately 33 participants) across the two strata (age <6 years and age ≥6 years). This sample size 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 – placebo) of 3.0. These calculations are based on α=0.05 (two-sided), a common standard deviation of 3.5 and using the normal approximation of the test statistic for the comparison between two means. Assuming both interim analyses will be performed (3 looks) and a gamma family alpha-spending function with gamma parameter -1 for efficacy will be used to control Type I error, the probability of crossing the boundary at the first interim analysis is 38%, at the second interim analysis is 78%, and at the primary analysis is 97%. A gamma family spending function with gamma parameter -4 will be used for the non-blinding futility boundary.

9.3. Populations for Analysis

For purposes of analysis, the following populations are defined:

Population	Description
Enrolled	All participants who sign the Informed Consent Document.
Randomly assigned to investigational product	All participants, excluding siblings, 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.
Efficacy Analysis Set (long-term)	All participants, including siblings, but excluding those meeting protocol exclusion criteria 15, who received a single dose of fordadistrogene movaparvovec (either at Year 1 or Year 2).
Safety Analysis Set (Cohort 2 delayed treatment)	All participants, including siblings, who received a single dose of fordadistrogene movaparvovec on Day 390 (Year 2 Day 1).
Safety Analysis Set (long-term)	All participants, including siblings and those meeting exclusion criterion 15, who received a single dose of fordadistrogene movaparvovec (either at Year 1 or Year 2).

[a] Of note, per the PCD definition in Sections 4.1 and 9.5, 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.

9.4. Statistical Analyses

The SAP will be developed and finalized before database lock and will describe all planned statistical analyses including the participant populations to be included in the analyses and procedures for accounting for missing, unused, and spurious data. This section is a summary of the planned statistical analyses of the primary and secondary endpoints.

9.4.1. Efficacy Analyses

Endpoint	Statistical Analysis Methods
Primary	Inferential testing for the primary analysis for the primary endpoint will be performed at α=0.05 (two-sided). Baseline NSAA total score is defined as the last non-missing NSAA total score collected prior to Year 1 IP administration. Primary analysis: Change from Baseline at Week 52 in the NSAA total score will be analyzed using a mixed model repeated measures approach including visits through Week 52 where NSAA is assessed. The analysis will be based on the FAS (Regardless of adherence to glucocorticoid regimen) and missing data will not be explicitly imputed. The model will include fixed effects for treatment (class variable), visit (class variable), treatment by visit interaction, Baseline NSAA total score (continuous variable), Screening age (continuous variable), Baseline NSAA total score by visit interaction, and Screening age by visit interaction with an unstructured covariance matrix to describe the correlation among different visits from the same participant. Alternative covariance structures to address any issues with model convergence will be specified in the SAP. To test the null hypothesis, estimates at Week 52 of the mean changes from Baseline 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. Sensitivity analyses to assess the effect of missing data will be described in the SAP.
Secondary	Inferential testing of the secondary endpoints will be performed as described in Section 9.1. Baseline is defined as the last non-missing assessment collected prior to Year 1 IP administration. The following endpoints will be analyzed using an analysis of covariance model including model terms for treatment group, Baseline (continuous variable), and Screening age (continuous variable). • Change from Baseline in percent normal mini-dystrophin expression level in biceps brachii muscle biopsies at Day 360 using LC-MS assay. • Change from Baseline in percent of muscle fibers expressing mini-dystrophin in biceps brachii muscle biopsies at Day 360 as assessed by immunofluorescence. Change from Baseline at Week 52 in serum CK concentration will be analyzed using a mixed model repeated measures approach and a log transformation. The model fixed effects will be similar to those in the primary endpoint analysis and visits through Week 52 where serum CK concentration is assessed will be included.

Endpoint	Statistical Analysis Methods
	The below two endpoints will be analyzed using a generalized mixed model assuming a binomial distribution and a logit link. The model terms will include treatment and Screening age (continuous variable). • Number of skills gained at Week 52 based on the individual items of the NSAA. For each individual item, a gained skill is defined as a score of 0 at Baseline and a score of 1 or 2 at Week 52. • Number of skills either improved or maintained at Week 52 compared to Baseline based on the individual items of the NSAA. For each individual item, an improved or maintained skill is defined as a score of 0 at Baseline and a score of 1 or 2 at Week 52, a score of 1 at Baseline and a score of 2 at Week 52, a score of 1 at Baseline and a score of 1 at Week 52, or a score of 2 at Baseline and a score of 2 at Week 52. The following endpoints will be analyzed using a similar mixed model repeated measures approach as used for the primary analysis. • 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; • 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).
Exploratory	Analyses for the exploratory endpoints defined in Section 3.1 will be described in the SAP.

As a general rule, all efficacy analyses including analysis of the primary endpoint, secondary endpoints, and other endpoints will be conducted based on FAS participants regardless of adherence to background or protocol mandated glucocorticoid regimens during the first 52 weeks after study drug infusion, unless specified otherwise.

9.4.2. Safety Analyses

All safety analyses will be performed on the safety population.

Statistical Analysis Methods

Descriptive summaries through Week 52 will be provided by treatment group for participants in the Safety (through Week 52) population for the following:
• Incidence, severity, and causal relationship of TEAEs (AEs and SAEs);
• Incidence of abnormal laboratory findings and magnitude of change;
• Abnormal and clinically relevant changes in:
  • Physical exam;
  • Neurological exam;
  • Weight;
  • Vital signs;
  • ECG;
  • Echocardiogram;
  • Cardiac MRI;
  • CBCL.

Descriptive summaries relative to pre-fordadistrogene movaparvovec baseline through Year 2 Week 52 for participants in the Safety (Cohort 2 delayed treatment) population will be provided for the above safety parameters.
Descriptive summaries relative to pre-fordadistrogene movaparvovec baseline through 5 years post fordadistrogene movaparvovec administration for participants in the Safety (long-term) population will be provided for the above safety parameters for combined Cohorts 1 and 2.

9.4.2.1. Electrocardiogram Analyses

Changes from Baseline through Week 52 for the ECG parameters QT interval, heart rate, QTc interval, PR interval, and QRS complex will be summarized by treatment and time. Changes in the above ECG parameters from pre-fordadistrogene movaparvovec baseline to Year 2 Week 52 for participants in Cohort 2 and at 1, 2, 3, 4 and 5 years post fordadistrogene movaparvovec administration will be summarized.

9.5. 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 primary analysis (Section 9.4.1). If either interim analysis is performed, a group sequential approach will be applied to the efficacy analyses to control Type I error 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.

Before any interim analysis is implemented, the details of the objectives, decision criteria (based on the actual number of participants and the number of looks), dissemination plan, method of maintaining the study blind, and analysis details will be recorded in the appropriate study documents. The interim analysis/analyses will be performed by an independent team of statisticians and programmers, and the results will be unblinded only to the E-DMC and/or a limited number of individuals within the Sponsor organization who are not involved in the conduct or further analysis of the ongoing study. These unblinded individuals from the Sponsor organization will be responsible for reviewing the results from the interim analyses and making a recommendation on pursuing a regulatory submission based on the interim analysis results.

The timing of public disclosure of the results of either interim analysis will be at the discretion of the Sponsor. If disclosure of interim analysis results prior to completion of the C3391003 trial is believed to have the potential to interfere with study completion, the Sponsor may choose to delay disclosure of the interim analysis until the trial has completed.

Irrespective of whether an interim analysis has been conducted, 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. . After the database has been released for the primary analysis, the study may become fully unblinded. If either an interim analysis is performed and the objectives are not met, the nominal type I error for the primary analysis will be adjusted accordingly. If either interim analysis is performed and the objective is met, the primary analysis at Week 52 will primarily be used to provide a more precise estimate of the treatment difference for the primary endpoint.

Additional analyses may be performed after the primary analysis, as needed, per regulatory requirements or in support of publications.

9.5.1. Data Monitoring Committee

This study will use an external data monitoring committee (E-DMC).

The E-DMC will be responsible for ongoing monitoring of the efficacy and safety of participants in the study according to the charter. The recommendations made by the E-DMC

to alter the conduct of the study will be forwarded to Pfizer for final decision. Pfizer will forward such decisions, which may include summaries of aggregate analyses of endpoint events and of safety data that are not endpoints, to regulatory authorities, as appropriate.

In the event of a serious safety issue, the Sponsor may determine that screening, randomization, and/or dosing are paused until the E-DMC reviews the relevant data and makes recommendations for the study conduct. CCI [redacted] Additional details on the E-DMC responsibilities can be found in the E-DMC Charter. The Sponsor will adhere to related local regulatory reporting requirements. If the trial is temporarily halted (screening, randomization, and/or dosing) by the Sponsor due to a safety concern (eg, in the event of a serious safety issue) the temporary halt notification must be submitted to the regulatory authorities within the regulatory timelines set in the current applicable regulations, and the trial restart will be only possible after regulatory approval via a substantial amendment, if needed.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and CIOMS International Ethical Guidelines;
- Applicable ICH GCP guidelines;
- Applicable laws and regulations, including applicable privacy laws.

The protocol, protocol amendments, ICD, SRSDs, and other relevant documents (eg, advertisements) must be reviewed and approved by the sponsor, and submitted to an IRB/EC by the investigator, and reviewed and approved by the IRB/EC before the study is initiated.

Any amendments to the protocol will require IRB/EC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

Protocols and any substantial amendments to the protocol will require health authority approval prior to initiation except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/EC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/EC;
- Notifying the IRB/EC of SAEs or other significant safety findings as required by IRB/EC procedures;
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH GCP guidelines, the IRB/EC, European regulation 536/2014 for clinical studies, European Medical Device Regulation 2017/745 for clinical device research, and all other applicable local regulations.

10.1.1.1. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the Investigator is aware of any new information that might influence the evaluation of the benefits and risks of the study intervention, Pfizer should be informed immediately. Investigators in Japan should see Section 10.10 (Appendix 10).

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the investigator becomes aware of.

10.1.2. Financial Disclosure

Investigators and subinvestigators will provide the Sponsor with sufficient, accurate financial information as requested to allow the Sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

10.1.3. Informed Consent Process

The investigator or their representative will explain the nature of the study to the participant and their parent(s)/legal guardian and answer all questions regarding the study. The participant and their parent(s)/legal guardian should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

When consent is obtained from a participant's parent(s)/legal guardian, the participant's assent (affirmative agreement) must be subsequently obtained when the participant has the capacity to provide assent, as determined by the IRB/EC. If the investigator determines that a participant's decisional capacity is so limited they cannot reasonably be consulted, then, as permitted by the IRB/EC and consistent with local regulatory and legal requirements, the participant's assent may be waived with source documentation of the reason assent was not obtained. If the study participant does not provide their own assent, the source documents must record why the participant did not provide assent (for example, the child is not of assenting age per local regulations or policies), how the investigator determined that the person signing the consent was the participant's parent(s)/legal guardian, the consent signer's relationship to the study participant, and that the participant's assent was obtained or waived. If assent is obtained verbally, it must be documented in the source documents.

If study participants are minors who reach the age of majority or if a child reaches the age of assent (per local IRB/EC requirements) during the study, as recognized under local law, the child or adolescent must then provide the appropriate assent or consent to document their willingness to continue in the study. For an adolescent who reaches the age of consent, parental consent would no longer be valid. If the enrollment of emancipated minors is permitted by the IRB/EC and local law, the participant must provide documentation of legal status to give consent without the permission of a legally authorized representative.

Participants and their parent(s)/legal guardian must be informed that their participation is voluntary. The participant's parent(s)/legal guardian will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, HIPAA requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each study participant's parent(s)/legal guardian and the study participant as applicable are fully informed about the nature and objectives of the study, the sharing of data related to the study, and possible risks associated with participation, including the risks associated with the processing of the participant's personal data.

The participant's parent(s)/legal guardian must be informed that the participant's personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant's parent(s)/legal guardian.

The participant's parent(s)/legal guardian must be informed that the participant's medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/EC members, and by inspectors from regulatory authorities.

The investigator further must ensure that each study participant's parent(s)/legal guardian is fully informed about their right to access and correct their child's personal data and to withdraw consent for the processing of their child's personal data, keeping in mind the privacy rights that may restrict access of older adolescents' medical records by their parent(s)/legal guardian in certain regions.

The source documentation must include a statement that written informed consent, and as applicable, assent was obtained before the participant was enrolled in the study and the date the written consent/assent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

Parent(s)/legal guardian and the participant must be reconsented to the most current version of the ICD(s)/assent during their participation in the study as required per local regulations.

A copy of the ICD(s) and assent, if written, must be provided to the parent(s)/legal guardian and the participant.

Participants who are rescreened are required to sign a new ICD.

10.1.4. Data Protection

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant data.

Participants' personal data will be stored at the study site in encrypted electronic and/or paper form and will be password protected or secured in a locked room to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site will be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of participants with regard to the processing of personal data, participants will be assigned a single, participant-specific numerical code. Any participant records or data sets that are transferred to the sponsor will contain the numerical code; participant names will not be transferred. All other identifiable data transferred to the sponsor will be identified by this single, participant-specific code. The study site will maintain a confidential list of participants who participated in the study, linking each participant's numerical code to their actual identity and medical record ID. In case of data transfer, the sponsor will protect the confidentiality of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

Information technology systems used to collect, process, and store study-related data are secured by technical and organizational security measures designed to protect such data against accidental or unlawful loss, alteration, or unauthorized disclosure or access.

The sponsor maintains SOPs on how to respond in the event of unauthorized access, use, or disclosure of sponsor information or systems.

10.1.5. Dissemination of Clinical Study Data

Pfizer fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT, and/or www.pfizer.com, and other public registries in accordance with applicable local laws/regulations. In addition, Pfizer reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

In all cases, study results are reported by Pfizer in an objective, accurate, balanced, and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

Pfizer posts clinical trial results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in patients) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT/CTIS

Pfizer posts clinical trial results on EudraCT/CTIS for Pfizer-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

www.pfizer.com

Pfizer posts CSR synopses and plain-language study results summaries on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the corresponding study results are posted to www.clinicaltrials.gov. CSR synopses will have personally identifiable information anonymized.

Documents within marketing applications

Pfizer complies with applicable local laws/regulations to publish clinical documents included in marketing applications. Clinical documents include summary documents and CSRs including the protocol and protocol amendments, sample CRFs, and SAPs. Clinical documents will have personally identifiable information anonymized.

Data Sharing

Pfizer provides researchers secure access to participant-level data or full CSRs for the purposes of "bona-fide scientific research" that contributes to the scientific understanding of the disease, target, or compound class. Pfizer will make data from these trials available 18 months after study completion. Participant-level data will be anonymized in accordance with applicable privacy laws and regulations. CSRs will have personally identifiable information anonymized.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

10.1.6. Data Quality Assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

Guidance on completion of CRFs will be provided in the CRF Completion Requirements document.

The investigator must ensure that the CRFs are securely stored at the study site in encrypted electronic and/or paper form and are password protected or secured in a locked room to prevent access by unauthorized third parties.

The investigator must permit study-related monitoring, audits, IRB/EC review, and regulatory agency inspections and provide direct access to source records and documents. This verification may also occur after study completion. It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

Monitoring details describing strategy, including definition of study-critical data items and processes (eg, risk based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, virtual, or on site monitoring), are provided in the data management plan and monitoring plan maintained and utilized by the sponsor or designee.

The sponsor or designee is responsible for the data management of this study, including quality checking of the data.

Records and documents, including signed ICDs, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor. The investigator must ensure that the records continue to be stored securely for as long as they are maintained.

When participant data are to be deleted, the investigator will ensure that all copies of such data are promptly and irrevocably deleted from all systems.

The investigator(s) will notify the sponsor or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with the sponsor or its agents to prepare the investigator site for the inspection and will allow the sponsor or its agent, whenever feasible, to be present during the inspection. The investigator site and investigator will promptly resolve any discrepancies that are identified between the study data and the participant's medical records. The investigator will promptly provide copies of the inspection findings to the sponsor or its agent. Before response submission to the regulatory authorities, the investigator will provide the sponsor or its agents with an opportunity to review and comment on responses to any such findings.

10.1.7. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the Investigator site. In most cases, the source documents are the hospital or the physician subject chart. In some cases, the CRF may also serve as the source document. In these cases, a document should be available at the investigator site and at Pfizer that clearly identifies those data that will be recorded on the CRF, and for which the CRF will stand as the source document.

Data reported on the CRF or entered in the electronic CRF (eCRF) that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The Investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

10.1.8. Use of Medical Records

In certain situations, sponsor review of redacted copies of participant medical records for local laboratory test results may be performed, where ethically and scientifically justified and permitted by local regulations, to ensure participant safety.

Due to the potential for a participant to be re-identified from their medical records, the following actions must be taken when medical records are sent to the sponsor or sponsor designee:

- The investigator or site staff must redact personal information from the medical record. The personal information includes, but is not limited to, the following: participant names or initials, participant dates (eg, birth date, date of hospital admission/discharge, date of death), participant identification numbers (eg, Social Security number, health insurance number, medical record number, hospital/institution identifier), participant location information (eg, street address, city, country, postal code, IP address), participant contact information (eg, telephone/fax number, email address).

- Each medical record must be transmitted to the sponsor or sponsor designee using systems with technical and organizational security measures to ensure the protection of personal data (eg, Florence is the preferred system if available).

- There may be unplanned situations where the sponsor may request medical records (eg, sharing medical records so that the sponsor can provide study-related advice to the investigator). The medical records should be submitted according to the procedure described above.

10.1.9. Study and Site Start and Closure

The study start date is the date of the first participant's first visit.

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor, including (but not limited to) regulatory authority decision, change in opinion of the IRB/EC, or change in benefit-risk assessment. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time upon notification to the CRO if requested to do so by the responsible IRB/EC or if such termination is required to protect the health of study participants.

Reasons for the early closure of a study site by the Sponsor may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/EC or local health authorities, the Sponsor's procedures, or GCP guidelines;

- Inadequate recruitment of participants by the investigator;

- Discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the ECs/IRBs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

If the sponsor decides to terminate the study for a reason unrelated to the safety of study intervention(s), protocol-specified safety assessments will continue to be performed for these participants until the end of the study as defined in Sections 4.4.

Study termination is also provided for in the clinical study agreement. If there is any conflict between the contract and this protocol, the contract will control as to termination rights.

10.1.10. Publication Policy

For multicenter trials, the primary publication will be a joint publication developed by the investigator and Pfizer reporting the primary endpoint(s) of the study covering all study sites. The investigator agrees to refer to the primary publication in any subsequent publications. Pfizer will not provide any financial compensation for the investigator's participation in the preparation of the primary congress abstract, poster, presentation, or primary manuscript for the study.

Investigators are free to publish individual center results that they deem to be clinically meaningful after publication of the overall results of the study or 12 months after primary completion date or study completion at all sites, whichever occurs first, subject to the other requirements described in this section.

The investigator will provide Pfizer an opportunity to review any proposed publication or any other type of disclosure of the study results (collectively, "publication") before it is submitted or otherwise disclosed and will submit all publications to Pfizer 30 days before submission. If any patent action is required to protect intellectual property rights, the investigator agrees to delay the disclosure for a period not to exceed an additional 60 days upon request from Pfizer. This allows Pfizer to protect proprietary information and to provide comments, and the investigator will, on request, remove any previously undisclosed confidential information before disclosure, except for any study-intervention or Pfizer-related information necessary for the appropriate scientific presentation or understanding of the study results. For joint publications, should there be disagreement regarding interpretation and/or presentation of specific analysis results, resolution of, and responsibility for, such disagreements will be the collective responsibility of all authors of the publication.

For all publications relating to the study, the Investigator and Pfizer will comply with recognized ethical standards concerning publications and authorship, including those established by the International Committee of Medical Journal Editors. The investigator will disclose any relationship with Pfizer and any relevant potential conflicts of interest, including any financial or personal relationship with Pfizer, in any publications. All authors will have

access to the relevant statistical tables, figures, and reports (in their original format) required to develop the publication.

10.1.11. Sponsor's Qualified Medical Personnel

The contact information for the Sponsor's appropriately qualified medical personnel for the study is documented in the study contact list located in the supporting study documentation provided by the Sponsor.

To facilitate access to appropriately qualified medical personnel on study-related medical questions or problems, participants are provided with a contact card. The contact card contains, at a minimum, protocol and investigational product identifiers, participant numbers, contact information for the Investigator site, and contact details for a contact center in the event that the Investigator site staff cannot be reached to provide advice on a medical question or problem originating from another healthcare professional not involved in the participant's participation in the study. The contact number can also be used by Investigator staff if they are seeking advice on medical questions or problems; however, it should be used only in the event that the established communication pathways between the Investigator site and the study team are not available. It is therefore intended to augment, but not replace, the established communication pathways between the Investigator site and the study team for advice on medical questions or problems that may arise during the study. The contact number is not intended for use by the participant directly, and if a participant calls that number, he will be directed back to the Investigator site.

10.2. Appendix 2: Clinical Laboratory Tests

The following safety laboratory tests will be performed at times defined in the SoA section of this protocol. Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory; or as derived from calculated values. These additional tests would not require additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety concerns.

Table 3. 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[a]	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)		

Table 3. Protocol Required Safety Laboratory Assessments

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	
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	
Local assessment of NT-ProBNP/BNP, if needed as per Section 8.2.7	
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 2
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

Table 3. Protocol Required Safety Laboratory Assessments

Haptoglobin (mandatory) **Other- prothrombin time, activated partial thromboplastin time, CRP, amylase, lipase (when possible)**	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
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 393 (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 393 (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 393 (Visits 21 and 22) in Year 2
GLDH	Day 9 (Visit 9) at Year 1 Day 398 (Visit 26) at Year 2 For sites in Japan additionally on Day 2 (Visit 4), Day 4 (Visit 5) in Year 1, and on Day 391 (Visit 21) and Day 393 (Visit 22) in 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 Day 42 (Visit 13.1) only for Germany) Day 431 (Visit 30.1 only for Germany)

Table 3. Protocol Required Safety Laboratory Assessments

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.

Any remaining biospecimens samples collected for clinical safety may be retained and stored for the duration of the study. Retained samples may be used for the assessment of exploratory biomarkers. These data will not be included in the clinical study report.

Investigators must document their review of each laboratory safety report.

Best Practice for Pediatric Blood Collection

Examples of best practices for pediatric blood collection which should be included in lab manuals and training materials include:

Ensure that the child is well-hydrated prior to blood collection.

Keep the child warm throughout the process of preparing for and drawing blood.

Engage caregivers to determine what is the most appropriate way to soothe their child.

- A lidocaine-based topical anesthetic (eg, lidocaine 4% cream) may be used prior to blood collection to decrease potential discomfort to the subject. The anesthetic must not contain propylene glycol (PG). The skin must be thoroughly cleansed prior to blood sample collection. It is recommended that two venipuncture sites be prepared with local anesthetic in case the first attempt is not successful.

- Adhere strictly to a limit on the number of venipuncture attempts in a pediatric participant. If no satisfactory sample has been collected after 2 attempts, seek a second opinion to decide whether to make a further attempt or cancel the tests.

10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting

10.3.1. Definition of AE

AE Definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. • NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events <u>Meeting</u> the AE Definition
• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the Investigator (ie, not related to progression of underlying disease). • Exacerbation of a chronic or intermittent preexisting condition including either an increase in frequency and/or intensity of the condition. • New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. • Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae. • "Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as an AE or SAE if they fulfill the definition of an AE or SAE.

Events NOT Meeting the AE Definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the Investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition. • Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.3.2. Definition of SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (eg, hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

An SAE is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.

An SAE is defined as any untoward medical occurrence that, at any dose:
Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.
d. Results in persistent disability/incapacity • The term disability means a substantial disruption of a person's ability to conduct normal life functions. • This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle) which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect
f. Other situations: • Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious. • Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse. • Suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic, is considered serious. The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a patient exposed to a Pfizer product. The terms "suspected transmission" and "transmission" are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance personnel. Such cases are also considered for reporting as product defects, if appropriate.

10.3.3. Recording/Reporting and Follow-up of AEs and/or SAEs

AE and SAE Recording/Reporting

The table below summarizes the requirements for recording adverse events on the CRF and for reporting serious adverse events on the Clinical Trial (CT) Serious Adverse Event (SAE) Report Form to Pfizer Safety. These requirements are delineated for 3 types of events: (1) SAEs; (2) nonserious adverse events (AEs); and (3) exposure to the investigational product under study during pregnancy or breastfeeding, and occupational exposure.

It should be noted that the CT SAE Report Form for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the CT SAE Report Form for reporting of SAE information.

Safety Event	**Recorded on the CRF**	**Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness**
SAE	All	All
Nonserious AE	All	None
Exposure to the investigational product under study during pregnancy or breastfeeding, and occupational exposure	All AEs/SAEs associated with exposure during pregnancy or breastfeeding Occupational exposure is not recorded	All (and exposure during pregnancy [EDP] supplemental form for EDP) Note: Include all SAEs associated with exposure during pregnancy or breastfeeding. Include all AEs/SAEs associated with occupational exposure.

- When an AE/SAE occurs, it is the responsibility of the Investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The Investigator will then record all relevant AE/SAE information in the CRF.
- It is **not** acceptable for the Investigator to send photocopies of the participant's medical records to Pfizer Safety in lieu of completion of the CT SAE Report Form/AE/SAE CRF page.

- There may be instances when copies of medical records for certain cases are requested by Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety.

- The Investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE.

Assessment of Intensity

The Investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: An event that is easily tolerated by the participant, causing minimal discomfort and not interfering with everyday activities.

- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.

- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; and both AEs and SAEs can be assessed as severe.

- An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

Assessment of Causality

- The Investigator is obligated to assess the relationship between study intervention and each occurrence of each AE/SAE.

- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.

- The Investigator will use clinical judgment to determine the relationship.

- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated.

Assessment of Causality

- The Investigator will also consult the Investigator's brochure (IB) and/or product information, for marketed products, in their assessment.
- For each AE/SAE, the Investigator **must** document in the medical notes that he/she has reviewed the AE/SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the Investigator has minimal information to include in the initial report to the Sponsor. However, **it is very important that the Investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the Sponsor.**
- The Investigator may change their opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.
- If the Investigator does not know whether or not the investigational product caused the event, then the event will be handled as "related to investigational product" for reporting purposes, as defined by the Sponsor. In addition, if the Investigator determines that an SAE is associated with study procedures, the Investigator must record this causal relationship in the source documents and CRF, and report such an assessment in the dedicated section of the CT SAE Report Form and in accordance with the SAE reporting requirements.

Follow-up of AEs and SAEs

- The Investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by the Sponsor to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare professionals.
- If a participant dies during participation in the study or during a recognized follow-up period, the Investigator will provide Pfizer Safety with a copy of any postmortem findings including histopathology.
- New or updated information will be recorded in the originally completed CRF.

Follow-up of AEs and SAEs
• The Investigator will submit any updated SAE data to the Sponsor within 24 hours of receipt of the information.

10.3.4. Reporting of SAEs

SAE Reporting to Pfizer Safety via an Electronic Data Collection Tool
• The primary mechanism for reporting an SAE to Pfizer Safety will be the electronic data collection tool. • If the electronic system is unavailable, then the site will use the paper SAE data collection tool (see next section) in order to report the event within 24 hours. • The site will enter the SAE data into the electronic system as soon as the data become available. • After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data. • If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to Pfizer Safety by telephone.
SAE Reporting to Pfizer Safety via CT SAE Report Form
• Facsimile transmission of the CT SAE Report Form is the preferred method to transmit this information to Pfizer Safety. • In circumstances when the facsimile is not working, notification by telephone is acceptable with a copy of the CT SAE Report Form sent by overnight mail or courier service. • Initial notification via telephone does not replace the need for the Investigator to complete and sign the CT SAE Report Form pages within the designated reporting time frames.

10.4. Appendix 4: Contraceptive and Barrier Guidance

10.4.1. Male Participant Reproductive Inclusion Criteria

The potential risk of exposure to fordadistrogene movaparvovec in a sexual partner of a male participant in this study via ejaculate is low, and therefore no contraception (condom) use in male participants is warranted.

10.5. Appendix 5: Genetics

Use/Analysis of DNA

- Genetic variation may impact a participant's response to study intervention, susceptibility to, and severity and progression of disease. Therefore, where local regulations and IRBs/ECs allow, a blood sample will be collected for DNA analysis.

- Genetic research may consist of the analysis of 1 or more candidate genes or the analysis of genetic markers throughout the genome or analysis of the entire genome (as appropriate).

- The samples may be analyzed as part of a multistudy assessment of genetic factors involved in the response to study intervention or study interventions of this class to understand treatments for the disease(s) under study or the disease(s) themselves.

- The results of genetic analyses may be reported in the clinical study report (CSR) or in a separate study summary, or may be used for internal decision making without being included in a study report.

- The Sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.

- The samples will be retained as indicated:

    - Samples for specified genetic analysis (see Section 8.7.1) will not be stored beyond the completion of this study (eg, CSR finalization).

    - Samples for banking (see Section 8.7.2 and Section 8.8.4) will be stored indefinitely or other period as per local requirements.

- Participants may withdraw their consent for the storage and/or use of their banked biospecimens at any time by making a request to the Investigator; in this case, any remaining material will be destroyed. Data already generated from the samples will be retained to protect the integrity of existing analyses.

- Banked biospecimens will be labeled with a code. The key between the code and the participant's personally identifying information (eg, name, address) will be held at the study site and will not be provided to the sample bank.

10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-up Assessments

Potential Cases of Drug Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed “tolerators,” while those who show transient liver injury, but adapt are termed “adaptors.” In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are "susceptible" to progressive and serious liver injury, commonly referred to as drug-induced liver injury (DILI). Participants who experience a transaminase elevation above 3 times the upper limit of normal (× ULN) should be monitored more frequently to determine if they are an “adaptor” or are “susceptible.”

In the majority of DILI cases, elevations in aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) precede total bilirubin (TBili) elevations (>2 × ULN) by several days or weeks. The increase in TBili typically occurs while AST/ALT is/are still elevated above 3 × ULN (ie, AST/ALT and TBili values will be elevated within the same laboratory sample). In rare instances, by the time TBili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to TBili that meet the criteria outlined below are considered potential DILI (assessed per Hy’s law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant’s individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy’s law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and TBili baseline values within the normal range who subsequently present with AST OR ALT values >3 × ULN AND a TBili value >2 × ULN with no evidence of hemolysis and an alkaline phosphatase value <2 × ULN or not available.

- For participants with baseline AST **OR** ALT **OR** TBili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

  Preexisting AST or ALT baseline values above the normal range: AST or ALT values >2 times the baseline values AND >3 × ULN; or >8 × ULN (whichever is smaller).

  Preexisting values of TBili above the normal range: TBili level increased from baseline value by an amount of at least 1 × ULN **or** if the value reaches >3 × ULN (whichever is smaller).

Rises in AST/ALT and TBili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy's law case should be reviewed with the Sponsor.

It is important to note that standard biomarkers for the onset of hepatocellular injury such as ALT and AST are difficult to interpret in patients with DMD, as they are also released from the diseased skeletal muscle. The criteria listed above for Hy's law in the setting of participants with baseline AST or ALT values above the ULN will be used, when applicable. GLDH, which is a liver-specific enzyme not elevated in patients with DMD, will be collected to aid in the evaluation of potential hepatocellular injury. Elevations of GLDH >2 x ULN will also be assessed individually, and participants who experience a consistent GLDH elevation above 3 × ULN may be monitored more frequently, based on the clinical judgment of the Investigator and with the assistance of the ad hoc hepatic and/or immunopharmacologic expert(s) supporting the E-DMC. Any case where uncertainty remains as to whether it represents a potential Hy's law case should be reviewed with the Sponsor.

The participant should return to the Investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history, and physical assessment.

In addition to repeating measurements of AST and ALT and TBili for suspected cases of Hy's law, additional laboratory tests should include albumin, creatine kinase (CK), direct and indirect bilirubin, gamma-glutamyl transferase (GGT), prothrombin time (PT)/international normalized ratio (INR), total bile acids, and alkaline phosphatase. Consideration should also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology. A detailed history, including relevant information, such as review of ethanol, acetaminophen (either by itself or as a coformulated product in prescription or over-the-counter medications), recreational drug, supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D, and E infection and liver imaging (eg, biliary tract) and collection of serum sample for acetaminophen drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and TBili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the liver function test (LFT) abnormalities has yet been found. **Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.**

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

10.7. Appendix 7: ECG Findings of Potential Clinical Concern

ECG Findings That May Qualify as Adverse Events (AEs)
• New prolongation of corrected QT (Fridericia method) (QTcF) to >480 msec (absolute) or by ≥60 msec from baseline.
ECG Findings That May Qualify as Serious Adverse Events (SAEs)
• QTcF prolongation >500 msec.
ECG Findings That Qualify as Serious Adverse Events
• Change in pattern suggestive of new myocardial infarction. • Sustained ventricular tachyarrhythmias (>30 seconds' duration). • Second- or third-degree AV block requiring pacemaker placement. • Asystolic pauses requiring pacemaker placement. • Atrial flutter or fibrillation with rapid ventricular response requiring cardioversion. • Ventricular fibrillation/flutter. • At the discretion of the Investigator, any arrhythmia classified as an adverse experience.

The enumerated list of major events of potential clinical concern are recommended as "alerts" or notifications from the core ECG laboratory to the Investigator and Pfizer study team, and not to be considered as all inclusive of what to be reported as AEs/SAEs.

10.8. Appendix 8: Country-Specific Requirements

10.8.1. France Contrat Unique

1. GCP Training

    a. Before enrolling any participants, the Investigator and any subinvestigators will complete the Pfizer-provided Good Clinical Practice training course ("Pfizer GCP Training") or training deemed equivalent by Pfizer. Any Investigators who later join the study will do the same before performing study-related duties. For studies of applicable duration, the Investigator and subinvestigators will complete Pfizer GCP Training or equivalent every 3 years during the term of the study, or more often if there are significant changes to the ICH GCP guidelines or course materials.

2. Investigational Product.

    b. No participants or third-party payers will be charged for investigational product.

3. Urgent Safety Measures.

    c. In addition, the Investigator will inform Pfizer immediately of any urgent safety measures taken by the Investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the Investigator becomes aware of.

4. Termination Rights.

    a. Pfizer retains the right to discontinue development of fordadistrogene movaparvovec at any time.

10.9. Appendix 9. Italy-Specific Country Amendment

This appendix is only for investigators in Italy.

10.9.1. Schedule of Activities

10.9.1.1. Schedule of Activities - Year 1 (Screening to Year 1 Day 360)

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [gg]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	
Informed consent/assent	X																					
Demography	X																					
Medical history	X[hh]																					
Medication history	X																					
Review of inclusion/exclusion criteria	X	X																				
Eligibility for Year 1 IP administration[v]			X																			
Hospital stay[ii]			X	→	→	→	→	X														
Physical examination[h]	X	X	X	X	X		X		X	X			X		X			X	X		X	X

Period	**Screening**	**Baseline**	**Main Study Period (Year 1)**																		**Early Discontinuation Visit[g]**
Visit Number/ Description	**Visit 1[a,b]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Approximate Blood Volume (ml)	**15**	**13.5**	**0**	**11**	**11**	**7**	**7**	**7**	**7**	**11**	**12**	**4.5**	**14**	**3.5**	**16**	**3.5**	**8**	**8**	**7**	**0**	**13**	
Neurological examination[h]	X	X			X		X		X	X			X		X			X	X		X	X
Weight		X											X					X	X	X	X	X
Height	X												X					X	X		X	X
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X		X			X	X		X	X
12-Lead ECG[k]	X		X				X			X											X	X
CBCL	X																				X	X[g]
Randomization		X[bb]																				
Laboratory Assessments[l]																						
Blood Samples																						
NAb	X	X[cc]											X								X	X[g]
ADA to mini-dystrophin and AAV9	X									X[ee]	X[ee]	X[ee]	X					X			X	X[g]

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	
ELISpot to mini-dystrophin and AAV9		X													X							X [g]
Viral Vector Shedding[z]	X			X	X						X				X		X	X	X		X	X [g]
Clinical safety (hematology, other)[l]	X			X	X					X	X		X		X		X	X	X		X	X [g]
Chemistry and hepatic safety[l]	X			X	X					X	X	X[dd]	X	X	X	X	X	X	X		X	X
Post IP intensified safety monitoring[l,w]				X	X					X	X		X									
Local and central laboratory testing[aa]		X		X	X	X	X	X	X													
Cardiac Troponin I	X										X	X	X	X	X	X	X	X			X	X

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a,b]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Approximate Blood Volume (ml)	**15**	**13.5**	**0**	**11**	**11**	**7**	**7**	**7**	**7**	**11**	**12**	**4.5**	**14**	**3.5**	**16**	**3.5**	**8**	**8**	**7**	**0**	**13**	
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																				X	
Biomarker (creatine kinase)[l]		X			X					X	X	X	X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[m]	X																		X		X	
Banked biospecimens for genetics[n]																	X					
Urine Samples																						
Clinical safety (urinalysis)[l]	X		X	X	X					X			X		X			X			X	X [g]

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a,b]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Approximate Blood Volume (ml)	**15**	**13.5**	**0**	**11**	**11**	**7**	**7**	**7**	**7**	**11**	**12**	**4.5**	**14**	**3.5**	**16**	**3.5**	**8**	**8**	**7**	**0**	**13**	
Banked biospecimens for biomarkers[m]	X																		X		X	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X		X		X	X	X		X	X[g]
Saliva Samples																						
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X		X		X	X	X		X	X[g]
Tissue Samples																						
Muscle biopsy[o]		X																			X[x]	
Imaging Assessments																						
Echocardiogram[p]	X																				X	X[g]
Cardiac MRI[ff]	X[gg]																				X[gg]	
Functional Assessments																						
FVC[q,y]	X																				X	X[g]
NSAA[q]	X	X													X			X	X		X	X
Ankle range of motion	X	X													X			X	X		X	X
Ambulatory status	X[r]														X			X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a,b]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Approximate Blood Volume (ml)	**15**	**13.5**	**0**	**11**	**11**	**7**	**7**	**7**	**7**	**11**	**12**	**4.5**	**14**	**3.5**	**16**	**3.5**	**8**	**8**	**7**	**0**	**13**	
Actigraphy[s]		X													X			X	X		X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI - Pediatric Parent[t]		X																	X		X	X
EQ-5D-Y Proxy[t]		X																			X	X
EQ-5D-5L		X																			X	X
PGIS:CG[t]		X													X			X	X		X	X
Participant-completed																						
EQ-5D-Y[t]																					X	X
Clinical evaluator-completed																						
CGIS[q]		X													X			X	X		X	X
Health economic questionnaires																						
HRU:CG		X																				
WPAI:DMD Caregiver		X																				
Interventions																						
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	X					

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a,b]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Approximate Blood Volume (ml)	**15**	**13.5**	**0**	**11**	**11**	**7**	**7**	**7**	**7**	**11**	**12**	**4.5**	**14**	**3.5**	**16**	**3.5**	**8**	**8**	**7**	**0**	**13**	
Background glucocorticoid regimen	X	X															X	→	→	→	→	
IP administration			X																			
Meningococcal vaccine	X	X																				
Ongoing monitoring																						
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate.

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:

- Schedule A:
  - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place immediately after or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.
- Schedule B:
  - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).
- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;
- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;
- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);

- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;
- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

b. **Visit 14** and **Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a).
- For sites outside the US, the Baseline visit must occur at least 45 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

l. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings, at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline Visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

x. All participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 9 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details please see Section 8.2.11 and Appendix 2.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post-IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. On Day 28 (Visit 12.2), only GLDH will be collected.

ee. ADA to mini-dystrophin only.

ff. The Investigator will discuss with the participant and caregiver the importance of having a baseline cardiac MRI, even under general anesthesia, to be able to assess and manage potential cardiac events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A Participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration

Period	Screening	Baseline	Main Study Period (Year 1)																		Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a,b]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	7	7	14	7	
Approximate Blood Volume (ml)	15	13.5	0	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	8	8	7	0	13	

(Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

gg. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

hh. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

ii. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

10.9.1.2. Schedule of Activities - Year 2 and Long-Term Follow Up

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	
Eligibility for Year 2 IP administration[r]	X																				
Hospital stay[dd]	X	→	→	→	→	X															
Physical examination[g]	X	X	X		X		X	X			X		X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X		X			X	X	X	X	X	X
Height and Weight											X					X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X		X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X										X		X	X
CBCL																		X	X	X	X[e]
Laboratory Assessments[k]																					
Blood Samples																					
NAb to AAV9											X							X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X					X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X												X							X[w]	X[e]
Viral Vector Shedding[u]								X					X		X	X	X			X	X[e]

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	
Clinical safety (hematology, other)[k]		X	X					X	X		X		X		X	X	X	X	X	X	X[e]
Chemistry and hepatic safety[k]								X	X	X[y]	X	X	X	X	X	X	X	X	X	X	X
Post IP intensified safety monitoring[k,s]		X	X					X	X		X										
Local and central laboratory testing[x]	X	X	X	X	X	X	X														
Cardiac Troponin I									X	X	X	X	X	X	X	X		X	X	X	X
Biomarker (creatine kinase)[k]			X					X	X	X	X	X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																	X	X			
Urine Samples																					
Clinical safety (urinalysis)[k]	X	X	X					X	X		X		X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																	X	X			
Viral Vector Shedding[u]					X				X				X		X	X	X	X		X	X[e]
Saliva Samples																					
Viral Vector Shedding[u]					X				X				X		X	X	X	X		X	X[e]

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	
Tissue Sample																					
Muscle Biopsy																				X[ee]	
Imaging Assessments																					
Echocardiogram[m]																		X		X	X[e]
Cardiac MRI[aa]																		X[aa]			
Functional Assessments																					
FVC[n,t]																		X		X	X[e]
NSAA[n]													X			X	X	X	X	X	X
Ankle range of motion													X			X	X	X	X	X	X
Ambulatory status													X			X	X	X	X	X	X
Actigraphy[o]													X			X	X	X	X	X	
Clinical Outcome Assessments																					
Caregiver-completed																					
Modified PODCI – Pediatric Parent[p]																	X	X	X	X	X
EQ-5D-Y Proxy[p]																		X		X	X
EQ-5D-5L																		X		X	X
PGIS:CG[p]													X			X	X	X	X	X	X
Participant-completed																					
Modified PODCI – Adolescent[p]																			X	X	X
EQ-5D-Y[p]																		X		X	X
PGIS[p]																			X	X	X

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	
Clinical evaluator-completed																					
CGIS[n]													X			X	X	X	X	X	X
Health economic questionnaires																					
HRU:CG																		X		X	X
WPAI:DMD Caregiver																		X		X	X
Study Interventions																					
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	X						
Background glucocorticoid regimen															X	→	→	→	X[v]	X[v]	
IP administration	X																				
Ongoing monitoring																					
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5 Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. **Visit 20 – Year 2, Week 1, Day 1**

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed **prior to IP administration**: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.
- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant´s Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel, see Appendix 16.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

b. **Visits 29, 29.2, 30.2, 31.2 and 32**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

c. **Visit 31** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. **Visit 42 and 43 – Long-term follow up Year 6**

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. **Early Discontinuation Visit**

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

f. **Visit Windows for Visits 20 through Visit 43**

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief **physical and neurological examinations,** as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

h. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

j. **12 Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

m. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

n. The **NSAA** and **CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. **An activity monitor** may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

p. **COAs** will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 , will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26 and 27. For more details please see Section 8.2.11 and Appendix 2.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Approximate Blood Volume (ml)	11.5	11	11	7	7	7	7	11	12	4.5	14	3.5	16	3.5	6	8	7	12	6	20	

y. On Day 417 (Visit 29.2), only GLDH will be collected.

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12, and Section 7.2.1.

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

ee. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

10.10. Appendix 10: Japan Appendix

This appendix is only for investigators in Japan.

10.10.1. Schedule of Activities

10.10.1.1. Schedule of Activities - Year 1 (Screening to Year 1 Day 360)

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [gg]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Informed consent/assent	X																						
Inform caregivers about study C3391007[dd]	X																						
Demography	X																						
Medical history	X[ii]																						
Medication history	X																						
Review of inclusion/exclusion criteria	X	X																					
Eligibility for Year 1 IP administration[v]			X																				
Hospital stay[jj]			X	→	→	→	→	X															
Physical examination[h]	X	X	X	X	X		X		X	X			X			X			X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Neurological examination[h]	X	X			X		X		X	X			X			X			X	X		X	X
Weight		X											X						X	X	X	X	X
Height	X												X						X	X		X	X
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X			X			X	X		X	X
12-Lead ECG[k]	X		X				X			X												X	X
CBCL	X																					X	X[g]
Randomization		X[bb]																					
Laboratory Assessments[l]																							
Blood Samples																							
NAb	X	(X)[cc]											X									X	X[g]
ADA to mini-dystrophin and AAV9	X									X[ff]	X[ff]	X[ff]	X						X			X	X[g]
ELISpot to mini-dystrophin and AAV9		X														X							X[g]

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Viral Vector Shedding[z]	X			X	X						X					X		X	X	X		X	X[g]
Clinical safety (hematology, other)[l]	X			X	X					X	X		X			X		X	X	X		X	X[g]
Chemistry and hepatic safety [l]	X			X	X					X	X	X[ee]	X		X	X	X	X	X	X		X	X
Post IP intensified safety monitoring[l,w]				X	X					X	X		X										
Local and central laboratory testing[aa]		X		X	X	X	X	X	X														
Cardiac Troponin I- central laboratory	X										X	X	X	X	X	X	X	X	X			X	X
Cardiac Troponin I or T-local laboratory		X		X	X	X		X[ll]	X														

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																					X	
Biomarker (creatine kinase)[l]		X			X					X	X	X	X		X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[m]	X																			X		X	
Banked biospecimens for genetics[n]																		X					
Urine Samples																							
Clinical safety (urinalysis)[l]	X		X	X	X					X			X			X			X			X	X[g]
Banked biospecimens for biomarkers[m]	X																			X		X	

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Saliva Samples																							
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Tissue Samples																							
Muscle biopsy[o]		X																				X[x]	
Imaging Assessments																							
Echocardiogram[p]	X																					X	X[g]
Cardiac MRI[gg]	X[hh]																					X[hh]	
Functional Assessments																							
FVC[q,y]	X																					X	X[g]
NSAA[q]	X	X														X			X	X		X	X
Ankle range of motion	X	X														X			X	X		X	X
Ambulatory status	X[r]															X			X	X		X	X
Actigraphy[s]		X														X			X	X		X	
Clinical Outcome Assessments																							
Caregiver-completed																							
Modified PODCI – Pediatric Parent[t]		X																		X		X	X
EQ-5D-Y Proxy[t]		X																				X	X
EQ-5D-5L		X																				X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
PGIS:CG[t]		X														X			X	X		X	X
Participant-completed																							
EQ-5D-Y[t]																						X	X
Clinical evaluator-completed																							
CGIS[q]		X														X			X	X		X	X
Health economic questionnaires																							
HRU:CG		X																					
WPAI:DMD Caregiver		X																					
Interventions																							
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X					
Background glucocorticoid regimen	X	X																X	→	→	→	→	
IP administration			X																				
Meningococcal vaccine	X	X																					
Ongoing monitoring																							
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
adverse event monitoring																							

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate.Schedule of Activities – Year 2 and Long-Term Follow Up

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;
- Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:
- Schedule A:
    - **First day:** collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place the next day or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.
- Schedule B:
    - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;
- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;
- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);
- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;
- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

b. **Visit 14** and **Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a);
- For sites outside the US, the Baseline visit should occur at least 31 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);
- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved . Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

l. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings, at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline Visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10. For sites in Japan: haptoglobin will be analyzed by the local laboratory on Days 2 and 4 (Visits 4 and 5).

x. All participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. See Section 8.8.5 for additional details.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 9 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details, please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 4 and 5, see Appendix 2 for details.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post IP administration. After that, the rate could

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details- please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. For US sites, only when approved by the relevant Institutional Review Board.

ee. On Day 28 (Visit 12.2), only GLDH will be collected.

ff. ADA to mini-dystrophin only.

gg. The Investigator will discuss with the participant and caregiver the importance of having a baseline cardiac MRI, even under general anesthesia to be able to assess and manage potential cardiac adverse events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A Participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

hh. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

ii. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

jj. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

kk. This visit is for sites in Germany only. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ll. Cardiac troponin I or T will be analyzed by the local laboratory only on Day 8 (Visit 8).

10.10.1.2. Schedule of Activities – Year 2 and Long Term Follow Up

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Eligibility for Year 2 IP administration[r]	X																					
Hospital stay[dd]	X	→	→	→	→	X																
Physical examination[g]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X			X			X	X	X	X	X	X
Height and Weight											X						X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X											X		X	X
CBCL																			X	X	X	X[e]
Laboratory Assessments[k]																						
Blood Samples																						
NAb to AAV9											X								X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X						X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X													X							X[w]	X[e]
Viral Vector Shedding[u]								X						X		X	X	X			X	X[e]

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Clinical safety (hematology, other)[k]		X	X					X	X		X			X		X	X	X	X	X	X	X[e]
Chemistry and hepatic safety[k]		X	X					X	X	X[y]	X		X	X	X	X	X	X	X	X	X	
Post IP intensified safety monitoring[k,s]		X	X					X	X		X											
Local and central laboratory testing[x]	X	X	X	X	X	X	X															
Cardiac Troponin I-central laboratory									X	X	X	X	X	X	X	X	X		X	X	X	X
Cardiac troponin I or T-local laboratory	X[ff]	X	X	X		X[gg]	X															
Biomarker (creatine kinase)[k]			X					X	X	X	X		X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																		X	X			
Urine Samples																						
Clinical safety (urinalysis)[k]	X	X	X					X	X		X			X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																		X	X			
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]

Period	**Year 2**																		**Long-term follow up**		**Early Discontinuation Visit [e]**
Visit Number/Description	**Visit 20[a,bb, cc]**	**Visit 21[bb, cc]**	**Visit 22[bb, cc]**	**Visit 23[bb, cc]**	**Visit 24[bb, cc]**	**Visit 25[bb, cc] & 26[bb, cc]**	**Visit 27[bb, cc]**	**Visit 28[bb, cc]**	**Visit 29[b, bb, cc]**	**Visit 29.2[b, bb, cc]**	**Visit 30[bb, cc]**	**Visit 30.1[cc ,bb,cc]**	**Visit 30.2[b, bb, cc]**	**Visit 31[c,cc]**	**Visit 31.2[b, cc]**	**Visit 32[b,cc]**	**Visit 33**	**Visit 34**	**Visit 35**	**Visits 36, 38, 40, 42[d]**	**Visits 37, 39, 41, 43[d]**	
	Year 2, Week 1, Day 1	**Year 2, Week 1, Day 2**	**Year 2, Week 1, Day 4**	**Year 2, Week 1, Day 6**	**Year 2, Week 1, Day 7**	**Year 2, Week 2, Days 8 &9**	**Year 2, Week 2, Day 10**	**Year 2, Week 2, Day 14**	**Year 2, Week 3**	**Year 2, Week 4**	**Year 2, Week 5**	**Year 2, Week 6**	**Year 2, Week 7**	**Year 2, Week 9**	**Year 2, Week 11**	**Year 2, Week 13**	**Year 2, Week 18**	**Year 2, Week 35**	**Year 2, Week 52**	**Years 3, 4, 5, 6[d]**	**Years 3, 4, 5, 6[d]**	
Visit Day	**390**	**391**	**393**	**395**	**396**	**397& 398**	**399**	**403**	**410**	**417**	**423**	**431**	**437**	**449**	**463**	**479**	**509**	**629**	**749**	**930, 1290, 1650, 2010[d]**	**1110, 1470, 1830, 2190[d]**	
Visit Window (± days)	**3[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f,c]**	**3[f]**	**3[f]**	**7[f]**	**7[f]**	**7[f]**	**30[f]**	**30[f]**	
Saliva Samples																						
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Tissue Sample																						
Muscle Biopsy																					X[hh]	
Imaging Assessments																						
Echocardiogram[m]																			X		X	X[e]
Cardiac MRI[aa]																			X[aa]			
Functional Assessments																						
FVC[n,t]																			X		X	X[e]
NSAA[n]														X			X	X	X	X	X	X
Ankle range of motion														X			X	X	X	X	X	X
Ambulatory status														X			X	X	X	X	X	X
Actigraphy[o]														X			X	X	X	X	X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI – Pediatric Parent[p]																		X	X	X	X	X
EQ-5D-Y Proxy[p]																			X		X	X
EQ-5D-5L																			X		X	X
PGIS:CG[p]														X			X	X	X	X	X	X
Participant-completed																						
Modified PODCI – Adolescent[p]																				X	X	X

Period	**Year 2**																		**Long-term follow up**		**Early Discontinuation Visit [e]**
Visit Number/Description	**Visit 20[a,bb, cc]**	**Visit 21[bb, cc]**	**Visit 22[bb, cc]**	**Visit 23[bb, cc]**	**Visit 24[bb, cc]**	**Visit 25[bb, cc] & 26[bb, cc]**	**Visit 27[bb, cc]**	**Visit 28[bb, cc]**	**Visit 29[b, bb, cc]**	**Visit 29.2[b, bb, cc]**	**Visit 30[bb, cc]**	**Visit 30.1[cc ,bb,cc]**	**Visit 30.2[b, bb, cc]**	**Visit 31[c,cc]**	**Visit 31.2[b, cc]**	**Visit 32[b,cc]**	**Visit 33**	**Visit 34**	**Visit 35**	**Visits 36, 38, 40, 42[d]**	**Visits 37, 39, 41, 43[d]**	
	Year 2, Week 1, Day 1	**Year 2, Week 1, Day 2**	**Year 2, Week 1, Day 4**	**Year 2, Week 1, Day 6**	**Year 2, Week 1, Day 7**	**Year 2, Week 2, Days 8 &9**	**Year 2, Week 2, Day 10**	**Year 2, Week 2, Day 14**	**Year 2, Week 3**	**Year 2, Week 4**	**Year 2, Week 5**	**Year 2, Week 6**	**Year 2, Week 7**	**Year 2, Week 9**	**Year 2, Week 11**	**Year 2, Week 13**	**Year 2, Week 18**	**Year 2, Week 35**	**Year 2, Week 52**	**Years 3, 4, 5, 6[d]**	**Years 3, 4, 5, 6[d]**	
Visit Day	**390**	**391**	**393**	**395**	**396**	**397& 398**	**399**	**403**	**410**	**417**	**423**	**431**	**437**	**449**	**463**	**479**	**509**	**629**	**749**	**930, 1290, 1650, 2010[d]**	**1110, 1470, 1830, 2190[d]**	
Visit Window (± days)	**3[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f,c]**	**3[f]**	**3[f]**	**7[f]**	**7[f]**	**7[f]**	**30[f]**	**30[f]**	
EQ-5D-Y[p]																			X		X	X
PGIS[p]																				X	X	X
Clinical evaluator-completed																						
CGIS[n]														X			X	X	X	X	X	X
Health economic questionnaires																						
HRU:CG																			X		X	X
WPAI:DMD Caregiver																			X		X	X
Study Interventions																						
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X						
Background glucocorticoid regimen																X	→	→	→	X[v]	X[v]	
IP administration	X																					
Ongoing monitoring																						
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. Visit 20 – Year 2, Week 1, Day 1

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);
- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed prior to IP administration: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately 1 to 4 hours prior to infusion of IP;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel, see Appendix 16.

b. Visits 29, 29.2, 30.2, 31.2, and 32

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

c. Visit 31 must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. Visit 42 and 43 – Long-term follow up Year 6

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. Early Discontinuation Visit

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

f. Visit Windows for Visits 20 through Visit 43

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief physical and neurological examinations, as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

h. O2 saturation will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. Vital signs will be measured 3 times per day during the inpatient stay post IP administration.

j. 12 Lead ECG will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. Clinical laboratory tests are described in detail in Table 3 (Appendix 2).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. Banked biospecimens for biomarkers are collected as described in Section 8.8.4.

m. Echocardiograms will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

n. The NSAA and CGIS will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. An activity monitor may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

p. COAs will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background glucocorticoid regimen. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10. For sites in Japan: haptoglobin will be analyzed by the local laboratory on Days 391 and 393 (Visits 21 and 22) in Year 2.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26 and 27. For more details please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 21 and 22, see Appendix 2 for details.

y. On Day 417 (Visit 29.2), only GLDH will be collected.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

ee. This visit is for sites in Germany only. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ff. Cardiac troponin I or T by the local laboratory to be collected pre-IP administration.

gg. Cardiac troponin I or T to be analyzed by the local laboratory only on Day 397 (Visit 25).

hh. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb, cc] & 26[bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc ,bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b, cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f,c]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the day of the visit for the biopsy at Visit 41.

10.10.2. Study Intervention Definition (per Japanese regulation)

Defect: Refers to lack of function of the study intervention (see Section 6.1), causing generally poor conditions where the cells cause adverse reactions that affects the human body) irrespective of what stage of manufacture, delivery, storage or use the defect occurs.

10.10.2.1. Reporting Criteria

Study intervention defects are to be reported to the sponsor within 24 hours of investigator awareness (see Section 10.10.1.2) if any of the points listed below apply. Note: The reporting of study intervention defects will not result in any change to the reporting of AEs as described in Section 10.3 (Appendix 3).

- Occurrence of study intervention defects directly or indirectly leads to SAE(s) (see Section 10.3.2) of a participant/user/other person.

OR

- Study intervention defects have not actually led to SAE(s) but may possibly lead to SAE(s) of a participant/user/other person.

For product complaints that do not meet the reporting criteria above, refer to the Investigational Product Complaints section of the study IP Manual for detailed reporting procedures.

10.10.2.2. Reporting Procedures

The following procedures are to be followed in order to report the Study Intervention Defect(s) to the Sponsor:

1. Study intervention defects information should be recorded, as completely as possible on the Investigational Drug Product (Regenerative medicine products) Complaint Submission Form located in the Investigator Site File.

The form should be submitted electronically lo sponsor within 24 hours of being aware of an intervention defect.

After the complaint is received by the Sponsor, a close out memo will be generated. This close out memo will be provided to the study site.

10.10.3. Study Design

In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post-IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be

further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post IP-administration). After this time, no limits to the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. Ongoing blinded review of safety data will be conducted by the study team, and frequent periodic unblinded reviews of safety data will be conducted by the E-DMC, as described in detail in the E-DMC charter. Sites in Japan must ensure at least 14 days between IP administration for consecutive participants.

10.10.4. Post IP Intensified Safety Monitoring (at Year 1 and Year 2)

Due to the potential for an immune reaction against the AAV9 vector and/or the transgene, participants will undergo an intensified safety monitoring period for the first 34 days after IP administration in Year 1 and in Year 2.

Following IP administration, participants will be monitored as inpatients for at least 7 days, or longer, if deemed necessary by the Investigator (see SoA for details). Participants must be in an individual room, ie, not shared with other patients. Volume status should be assessed regularly, and if a participant experiences nausea or vomiting, consideration should be given to the placement of an IV line for treatment with an IV anti-emetic, hydration and replacement of the oral protocol-mandated glucocorticoid regimen by an IV regimen (see Section 6.5.1). Upon discharge, participants will be asked to stay local to the site (ie, if they do not live near the site, they will be asked to stay in at an overnight facility) for at least 14 days, or longer, if deemed necessary by the Investigator. Participants randomized from sites in Japan will be admitted to hospital for at least 14 days after IP administration and will be discharged if there are no ongoing adverse events that require medical management. On the day of IP administration, if adverse events possibly related to IP administration are observed, participants should not be discharged until the events have resolved.

10.10.5. Regulatory Reporting Requirements for SAEs

The sponsor will report SAEs that impact study status, or were deemed life-threatening, to the Japan sites within approximately 24 hours of Pfizer Japan receipt of the report.

10.10.6. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the investigational product, Pfizer should be informed immediately. This information should be shared with Japan sites approximately 24 hours after Pfizer Japan is aware of this information.

10.10.7. Study Intervention(s) Administered

Intervention Name	fordadistrogene movaparvovec	Placebo for fordadistrogene movaparvovec
Type	Gene Therapy	Placebo for Gene Therapy
Use	Experimental	Placebo
IMP and NIMP/AxMP	IMP	IMP
Dose Formulation	Sterile Solution for Infusion	Sterile Solution for Infusion
Unit Dose Strength(s)	1E14 vg/mL Note: This is the nominal concentration of the IP; for lot specific dosing calculation, the exact strength of each lot will be provided. For nominal dosing, 1E14 vg/mL will be the concentration used for the calculation of the administered dose. Nominal dosing will only be implemented for Year 2 IP administration. The Sponsor will communicate to the sites what dosing strategy must be implemented for each participant to be dosed. (Refer to IP Manual for further details)	0 vg/mL
Dosage Level(s)	2E14 vg/kg Single dose IV infusion	0 vg/kg Single dose IV infusion
Route of Administration	Intravenous Infusion	Intravenous Infusion
Sourcing	Provided centrally by the Sponsor (Refer to IP Manual for further details)	Provided centrally by Sponsor (Refer to IP Manual for further details)
Packaging and Labeling	Study intervention will be provided as 5 mL per vial (5 mL/vial). Each vial will be labeled as required per country requirement	Study intervention will be provided as 5 mL per vial (5 mL/vial). Each vial will be labeled as required per country requirement
SRSD	IB	IB

Study Intervention(s)						
Intervention Name	IV methylprednisolone	Oral prednisone or prednisolone	Deflazacort	Eculizumab	Antiemetics eg. ondansetron	MenACWY Vaccine
Type	Drug	Drug	Drug	Drug	Drug	Vaccine
Use	One-time, pre-administration of IP, Year 1 and Year 2	Background glucocorticoid regimen pre- IP administration and after completion of 90-day Protocol-mandated glucocorticoid regimen for at least the first 2 years in the study. Protocol-mandated post-IP dosing for 90 days	Background glucocorticoid regimen pre- IP administration and after completion of 90-day Protocol-mandated glucocorticoid regimen for at least the first 2 years in the study	Medication to treat adverse events (aHUS), to be administered at the discretion of the Investigator. Guidance for use provided in Section 6.5.1	Medication to prevent or treat adverse events (nausea and/or vomiting), to be administered at discretion of Investigator. See Section 6.5.1	Required per eculizumab label. Must be administered no later than 30 days before and only after 60 post- IP administration. See Section 6.5.1
IMP or NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP	NIMP/AxMP
Dose Formulation	Sterile solution for injection	Tablets or Oral Suspension	Tablet or Oral suspension	Sterile Solution for Infusion	Orally disintegrating tablet or sterile solution for injection	Solution for injection
Unit Dose Strength(s)	40 mg/mL	1 mg, 2 mg or 5 mg	Tablets: 6 mg, 18 mg, 30 mg or 36 mg Oral Suspension: 22.75 mg/mL	300 mg concentrate (10 mg/ml)	Tablet: 4 mg or 8 mg Injection: 2mg/mL	10 mcg group A, 5 mcg group C, 5 mcg group W-135, 5 mcg group Y
Dosage Level(s)	2 mg/kg	At least 0.5 mg/kg/day	At least 0.75 mg/kg/day	Total dose to be determined by the investigator	Total dose to be determined by the investigator	Single dose injection (0.5mL)
Route of Administration	Intravenous infusion	Oral	Oral	Intravenous Infusion	Oral/ injection/IV infusion	Intramuscular injection

Study Intervention(s)						
Sourcing	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	The sponsor will provide initial safety stock then remaining supply to be sourced by the clinical site using locally approved product unless otherwise arranged with the sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor	Sourced by the clinical site using locally approved product or provided to the site by local vendors coordinated by the Sponsor
Packaging and Labeling	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as 300 mg/30mL (10mg/mL) vial concentrated solution for intravenous infusion. Product will be labeled as required per country and site requirements.	Study intervention will be provided as locally approved product and labeled as required per country and site requirements	Study intervention will be provided as locally approved product and labeled as required per country and site requirements
SRSD	SmPC	SmPC	SmPC	SmPC	SmPC	SmPC

Of the study interventions listed in the table above: IV methylprednisolone, oral prednisone, or prednisolone, deflazacort, eculizumab, antiemetics e.g., ondansetron and MenACWY vaccine are not subject to safety reporting in accordance with Japanese regulation requirements.

10.10.8. Clinical Laboratory Tests

Table 4. 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[a]	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 4. 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	
Local assessment of NT-ProBNP/BNP, if needed as per Section 8.2.7	
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 2
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 (mandatory) **Other- prothrombin time activated partial thromboplastin time, CRP, amylase, lipase** (when possible)	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

Table 4. Protocol Required Safety Laboratory Assessments

Central Laboratory	
Clinical safety (not for Japan)	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 393 (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 393 (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 393 (Visits 21 and 22) in Year 2
GLDH	Day 9 (Visit 9) at Year 1 Day 398 (Visit 26) at Year 2 For sites in Japan additionally on Day 2 (Visit 4), Day 4 (Visit 5) in Year 1, and on Day 391 (Visit 21) and Day 393 (Visit 22) in 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 Day 42 (Visit 13.1) only for Germany) Day 431 (Visit 30.1 only for Germany)

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.

10.11. Appendix 11: Alternative Measures During Public Emergencies

The alternative study measures described in this section are to be followed during public emergencies, including the COVID-19 pandemic. This appendix applies for the duration of the COVID-19 pandemic and will become effective for other public emergencies only upon written notification from Pfizer.

Use of these alternative study measures are expected to cease upon the return of business as usual circumstances (including the lifting of any quarantines and travel bans/advisories).

10.11.1. Telehealth Visits

In the event that in-clinic study visits cannot be conducted, every effort should be made to follow-up on the safety of study participants at scheduled visits per the SoA or unscheduled visits. Telehealth visits may be used, if/when it is not possible to have home visits conducted by a home healthcare service (see Section 10.11.3), to continue to assess participant safety and collect data points. Telehealth includes the exchange of healthcare information and services via telecommunication technologies (eg, audio, video, video-conferencing software) remotely, allowing the participant and the investigator to communicate on aspects of clinical care, including medical advice, reminders, education, and safety monitoring. The following assessments must be performed during a telehealth visit:

- Review and record any AEs and SAEs since the last contact. Refer to Section 8.3.
- Review and record any new concomitant medications or changes in concomitant medications since the last contact.

Study participants must be reminded to promptly notify site staff about any change in their health status.

10.11.2. Alternative Facilities for Safety Assessments

10.11.2.1. Laboratory Testing

If a study participant is unable to visit the site for protocol-specified safety laboratory evaluations, testing may be conducted at a local laboratory if permitted by local regulations. The local laboratory may be a standalone institution or within a hospital. The following safety laboratory evaluations may be performed at a local laboratory (see Appendix 2):

- Hematology panel
- Chemistry panel; please note that the results of CK, AST and ALT should not be made available to the study site and Sponsor (see Section 6.3.3)
- Urinalysis
- Other (as defined in Table 3 in Appendix 2).

If a local laboratory is used, qualified study site personnel must order, receive, and review results. Site staff must collect the local laboratory reference ranges and certifications/accreditations for filing at the site. Laboratory test results are to be provided to the site staff as soon as possible. The local laboratory reports should be filed in the participant's source documents/medical records. Relevant data from the local laboratory report should be recorded on the CRF.

10.11.3. Home Health Visits

A home health care service will be utilized to facilitate scheduled visits per the SoA. Home health visits include a healthcare provider conducting an in-person study visit at the participant's location, rather than an in-person study visit at the site. The following may be performed during a home health visit:

- Blood draws
- Urine sample collection
- Vital signs

10.12. Appendix 12: Retrospective Assessment of Exclusion Criterion 15

10.12.1. Retrospective Assessment of Original Exclusion Criterion 15

Original exclusion criterion 15:

1. Participants with the following genetic abnormalities in the dystrophin gene as confirmed by the investigator based on the review of DMD genetic testing:

    a. Any mutation (exon deletion, exon duplication, insertion, or point mutation) affecting any exon between exon 9 and exon 13, inclusive; OR

    b. A deletion that affects both exon 29 and exon 30.

For participants who had started, or completed the Screening Visit (Visit 1), but were not randomized, exclusion criterion 15 will be assessed as part of the study eligibility assessment.

For participants randomized, but who have not yet received IP, the investigator will review the results of the genetic testing, and will withdraw from the study any participant who meets exclusion criterion 15 (see Section 7.2).

For participants who have already received IP, the unblinded medical monitor will review the results of the genetic testing to determine that:

2. Participants in Cohort 1 who meet exclusion criterion 15 will remain in the study for safety monitoring; but will not receive placebo in Year 2 (Section 7.1). Therefore, these participants will not require the post-IP safety monitoring in Year 2, will not attend Visit 18 in Year 1 and Visits 20 to 30.2 in Year 2, but will attend all subsequent visits; they will not receive their protocol-mandated glucocorticoid regimen in Year 2. Please find additional details in Sections 1.3.1; 1.3.2; 5.2; 6.5.1; 6.5.2; 7.1; and 8.2.10.

3. Participants in Cohort 2 who meet exclusion criterion 15 will be confirmed to be not eligible for Year 2 IP administration and will be withdrawn from the study immediately upon determination of ineligibility.

10.12.2. Retrospective Assessment of Updated Exclusion Criterion 15

Updated exclusion criterion 15:

1. Participants with the following genetic abnormalities in the dystrophin gene as confirmed by the investigator based on the review of DMD genetic testing:

    a. Any mutation (exon deletion, exon duplication, insertion, or point mutation) affecting any exon between exon 9 and exon 13, inclusive; OR

    b. A deletion that affects both exon 29 and exon 30; OR

    c. A deletion that affects any exons between 56-71, inclusive.

- For current study participants who have not yet received investigational product (ie, those screened/randomized but not dosed) the investigator will review the results of the genetic test and determine if the updated exclusion criterion 15 is met.
    - Participants screened but not randomized who meet the updated exclusion criterion 15 must be screen failed.
    - Participants randomized but not dosed who meet the updated exclusion criterion 15 must be discontinued from the study.
    - Participants screened/randomized but not dosed who do not meet the updated exclusion criterion 15 will continue with the protocol visits and procedures.
- For participants who have already received Year 1 IP, (but not Year 2 IP), the unblinded medical monitor will review the results of the genetic testing to determine that:
    - Participants in Cohort 1 who meet the newly defined exclusion criterion 15 will remain in the study for safety monitoring but will not receive placebo in Year 2 (see Section 7.1). Therefore, these participants will not require the post-IP safety monitoring in Year 2, will not attend Visit 18 in Year 1 and Visits 20 to 30.2 in Year 2, but will attend all subsequent visits; they will not receive their protocol-mandated glucocorticoid regimen in Year 2. Please find additional details in Section 1.3.1; Section 1.3.2; Section 5.2; Section 6.5.1; Section 6.5.2; Section 7.1; and Section 8.2.10.
    - Participants in Cohort 2 who meet exclusion criterion 15 will be confirmed to be not eligible for Year 2 IP administration and will be withdrawn from the study immediately upon determination of ineligibility.
- Participants who have already received Year 2 IP will remain in the study even if the investigator confirms that the updated exclusion criterion 15 is met. In that case a very close follow up for signs/symptoms of myositis will be performed, especially during the first 3 months post IP administration.

10.13. Appendix 13: DMD Long-Term Safety and Effectiveness Follow-Up PASS Study

To evaluate the longer term safety and efficacy of fordadistrogene movaparvovec, the sponsor plans to conduct a post-approval, non-interventional Registry study. Participants in the Registry will include participants who have completed 5 years of follow-up post administration of fordadistrogene movaparvovec in any of the sponsor studies (Phase 1b, 2, or 3), and newly treated patients in the post-marketing setting. The sponsor anticipates that the follow up in the post-approval Registry study will be 10 years and therefore participants treated within a sponsor study would be followed for a total of 15 years after dosing with fordadistrogene movaparvovec, while patients treated in the post-marketing setting will have 10 years of follow up.

Safety and efficacy information is expected to be collected on a yearly basis, and may include demographic information, assessment of muscle strength, ambulation status, the NSAA to assess lower limb function, the PUL 2.0 to assess upper limb function, ventilation status, pulmonary function testing, and evaluation of cardiac function with echocardiogram or cardiac MRI.

Details of this study will be included in a separate protocol.

10.14. Appendix 14: Germany-Specific Country Amendment

This appendix is only for investigators in Germany.

10.14.1. Schedule of Activities – Year 1

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Informed consent/assent	X																						
Inform caregivers about study C3391007[dd]	X																						
Demography	X																						
Medical history	X[ii]																						
Medication history	X																						
Review of inclusion/exclusion criteria	X	X																					
Eligibility for Year 1 IP administration[v]			X																				
Hospital stay[jj]			X	→	→	→	→	X															
Physical examination[h]	X	X	X	X	X		X		X	X			X			X			X	X		X	X
Neurological examination[h]	X	X			X		X		X	X			X			X			X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Weight		X											X						X	X	X	X	X
Height	X												X						X	X		X	X
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X			X			X	X		X	X
12-Lead ECG[k]	X		X				X			X												X	X
CBCL	X																					X	X [g]
Randomization		X[bb]																					
Laboratory Assessments[l]																							
Blood Samples																							
Nab	X	(X)[cc]											X									X	X [g]
ADA to mini-dystrophin and AAV9	X									X[ff]	X[ff]	X[ff]	X						X			X	X [g]
ELISpot to mini-dystrophin and AAV9		X														X							X [g]
Viral Vector Shedding[z]	X			X	X						X					X		X	X	X		X	X [g]

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Clinical safety (hematology, other)[l]	X			X	X					X	X		X			X		X	X	X		X	X[g]
Chemistry and hepatic safety [l]	X			X	X					X	X	X[ee]	X		X	X	X	X	X	X		X	X
Post IP intensified safety monitoring[l,w]				X	X					X	X		X										
Local and central laboratory testing[aa]		X		X	X	X	X	X	X														
Cardiac Troponin I	X										X	X	X	X	X	X	X	X	X			X	X
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																					X	
Biomarker (creatine kinase) [l]		X			X					X	X	X	X		X	X	X	X	X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Banked biospecimens for biomarkers[m]	X																			X		X	
Banked biospecimens for genetics[n]																		X					
Urine Samples																							
Clinical safety (urinalysis)[l]	X		X	X	X					X			X			X			X			X	X[g]
Banked biospecimens for biomarkers[m]	X																			X		X	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Saliva Samples																							
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Tissue Samples																							
Muscle biopsy[o]		X																				X[x]	
Imaging Assessments																							
Echocardiogram[p]	X																					X	X[g]
Cardiac MRI[gg]	X[hh]																					X[hh]	

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Functional Assessments																							
FVC[q,y]	X																					X	X[g]
NSAA[q]	X	X														X			X	X		X	X
Ankle range of motion	X	X														X			X	X		X	X
Ambulatory status	X[r]															X			X	X		X	X
Actigraphy[s]		X														X			X	X		X	
Clinical Outcome Assessments																							
Caregiver-completed																							
Modified PODCI – Pediatric Parent[t]		X																		X		X	X
EQ-5D-Y Proxy[t]		X																				X	X
EQ-5D-5L		X																				X	X
PGIS:CG[t]		X														X			X	X		X	X
Participant-completed																							
EQ-5D-Y[t]																						X	X
Clinical evaluator-completed																							
CGIS[q]		X														X			X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Health economic questionnaires																							
HRU:CG		X																					
WPAI:DMD Caregiver		X																					
Interventions																							
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X					
Background glucocorticoid regimen	X	X																X	→	→	→	→	
IP administration			X																				
Meningococcal vaccine	X	X																					
Ongoing monitoring																							
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; Nab=neutralizing antibodies;

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1 [kk]	Visit 13.2 [e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate.Schedule of Activities – Year 2 and Long-Term Follow Up

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;
- Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:
- Schedule A:
    - **First day:** collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, Nab to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place the next day or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.
- Schedule B:
    - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).
- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;
- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1 [kk]	Visit 13.2 [e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);
- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;
- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

b. **Visit 14 and Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a);
- For sites outside the US, the Baseline visit should occur at least 31 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);
- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved . Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).
- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

l. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings, at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

x. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. See Section 8.8.5 for additional details.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details, please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 4 and 5, see Appendix 2 for details.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details- please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. For US sites, only when approved by the relevant Institutional Review Board.

ee. On Day 28 (Visit 12.2), only GLDH will be collected.

ff. ADA to mini-dystrophin only.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

gg. The Investigator will discuss with the participant and caregivers the importance of having a baseline cardiac MRI, even under general anesthesia, to be able to assess and manage potential cardiac adverse events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

hh. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

ii. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

jj. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

kk. This visit is for sites in Germany only and only to test for cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

10.14.2. Schedule of Activities – Year 2

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[,bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Eligibility for Year 2 IP administration[r]	X																					
Hospital stay[dd]	X	→	→	→	→	X																
Physical examination[g]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X			X			X	X	X	X	X	X
Height and Weight											X						X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X											X		X	X
CBCL																			X	X	X	X[e]
Laboratory Assessments[k]																						
Blood Samples																						
NAb to AAV9											X								X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X						X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X													X							X[w]	X[e]
Viral Vector Shedding[u]								X						X		X	X	X			X	X[e]
Clinical safety (hematology, other)[k]		X	X					X	X		X			X		X	X	X	X	X	X	X[e]

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[b,bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Chemistry and hepatic safety[k]		X	X					X	X	X[y]	X		X	X	X	X	X	X	X	X	X	
Post IP intensified safety monitoring[k,s]		X	X					X	X		X											
Local and central laboratory testing[x]	X	X	X	X	X	X	X															
Cardiac Troponin I									X	X	X	X	X	X	X	X	X		X	X	X	X
Biomarker (creatine kinase) [k]			X					X	X	X	X		X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																		X	X			
Urine Samples																						
Clinical safety (urinalysis) [k]	X	X	X					X	X		X			X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																		X	X			
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Saliva Samples																						
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Tissue Sample																						
Muscle Biopsy																					X[ff]	
Imaging Assessments																						
Echocardiogram[m]																			X		X	X[e]
Cardiac MRI [aa]																			X[aa]			
Functional Assessments																						

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
FVC[n,t]																			X		X	X[e]
NSAA[n]														X			X	X	X	X	X	X
Ankle range of motion														X			X	X	X	X	X	X
Ambulatory status														X			X	X	X	X	X	X
Actigraphy [o]														X			X	X	X	X	X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI – Pediatric Parent[p]																		X	X	X	X	X
EQ-5D-Y Proxy[p]																			X		X	X
EQ-5D-5L																			X		X	X
PGIS:CG[p]														X			X	X	X	X	X	X
Participant-completed																						
Modified PODCI – Adolescent[p]																				X	X	X
EQ-5D-Y[p]																			X		X	X
PGIS[p]																				X	X	X
Clinical evaluator-completed																						
CGIS[n]														X			X	X	X	X	X	X
Health economic questionnaires																						
HRU:CG																			X		X	X
WPAI:DMD Caregiver																			X		X	X
Study Interventions																						
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X						

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Background glucocorticoid regimen																X	→	→	→	X[v]	X[v]	
IP administration	X																					
Ongoing monitoring																						
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5 Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. **Visit 20 – Year 2, Week 1, Day 1**

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);
- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed **prior to IP administration**: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[b,bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.
- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel, see Appendix 16 .

b. **Visits 29, 29.2, 30.2, 31.2, and 32**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

c. **Visit 31** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. **Visit 42 and 43 – Long-term follow up Year 6**

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. **Early Discontinuation Visit**

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

f. **Visit Windows for Visits 20 through Visit 43**

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief **physical and neurological examinations,** as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

h. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

j. **12 Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

m. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

n. The **NSAA** and **CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. **An activity monitor** may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[cc,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

p. **COAs** will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26 and 27. For

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

more details please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 21 and 22, see Appendix 2 for details.

y. On Day 417 (Visit 29.2), only GLDH will be collected.

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

ee. This visit is for sites in Germany only and only to test for cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ff. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

10.14.3. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

1. Male participants who are ≥4 and <8 years of age at Screening (Visit 1).

2. Confirmed diagnosis of DMD by prior genetic testing demonstrating the presence of a mutation in the dystrophin gene consistent with DMD at Screening (Visit 1). If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1).

3. Receipt of a stable daily dose of glucocorticoids (≥0.5 mg/kg/day prednisone, prednisolone, or ≥0.75 mg/kg/day deflazacort) for at least 3 months prior to Screening (Visit 1) and during the period between Screening (Visit 1) and Day 1 (Visit 3). In order to comply with protocol procedures, there should also be a reasonable expectation that this daily dose of glucocorticoids will remain stable for the first 2 years of the study. A stable dose is defined as one in which any change is ≤0.2 mg/kg (See Section 6.5.1 for detailed requirements).

4. A NSAA total score >16 and <30 at Screening (Visit 1).

5. Ambulatory, defined as being able to walk 10 meters unassisted, at Screening (Visit 1).

6. Participants/legally acceptable representatives who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures including, potentially, open muscle biopsies under general anesthesia and cardiac MRI under general anesthesia.

7. Participants/legally acceptable representatives who are capable of giving assent/signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the assent/informed consent document (ICD) and in this protocol.

8. Participants/legally acceptable representatives who are willing to protect the integrity of the study data by not actively seeking sensitive clinical data (eg, CK, ALT, AST, NAb to AAV9) through independent laboratory tests and by not sharing trial experiences with other participants or publicly (eg, through social media).

9. **For sites in Germany only:** At the Screening Visit (Visit 1), the investigator will discuss and agree with the participant or their legally acceptable representative the potential need for an autopsy, if the participant dies between Year 1 IP administration and during the following 10 years.

10.14.4. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

1. Prior treatment with gene therapy, defined as any therapy introducing exogenous DNA or intended to permanently alter the endogenous DNA. Gene therapy (other than IP) will be prohibited for the duration of the study.

2. Exposure within 6 months prior to Screening (Visit 1) to any treatment designed to increase dystrophin expression (including, but not limited to exon-skipping and nonsense read-through). These treatments will also be prohibited during the period between Screening (Visit 1) and Day 1 (Visit 3) and for the first 52 weeks of the study. Please note that for participants who are eligible for these treatments:

   Participants may be enrolled who have previously experienced lack of efficacy, or intolerance, as long as they received their last dose more than 6 months before screening (Visit 1), or who have refused these treatments.

   Participants receiving these treatments from which there is believed to be benefit should not discontinue them in order to meet this exclusion criterion and enroll in the study.

3. Previous administration with an investigational drug or investigational vaccine within 30 days (or as determined by the local requirement) or 5 half-lives (whichever is longer) at Screening (Visit 1). These treatments will also be prohibited during the period between Screening (Visit 1) and Day 1 (Visit 3) and for the first 2 years of the study.

4. Known cognitive impairment or behavioral issues that would impede the ability to follow instructions, in the judgment of the Investigator, at Screening (Visit 1).

5. Any nonhealed injury at Screening (Visit 1) which, in the opinion of the Investigator, may impact functional testing; additionally, lower limb fractures must have been healed for at least 3 months prior to Screening (Visit 1).

6. Positive test for NAb to AAV9, based on the threshold determined by the Central Laboratory, from a sample taken at Screening (Visit 1).

7. Receipt of a live attenuated vaccination within 30 days prior to Screening (Visit 1). Receipt of a live attenuated vaccination will also be prohibited for 90 days before Day 1 (Visit 3), for 90 days prior to Year 2 IP administration, and for the first 2 months after each IP administration.

8. Abnormality in hematology or chemistry profiles at Screening (Visit 1). A single repeat for value(s) outside allowable limits is permitted to re-assess eligibility:

   a. Absolute neutrophil count <1000 cells/mm^3;

b. Platelets <150 x 10^3/µl;

c. Cystatin C >1.2 x ULN;

d. Positive hepatitis A virus (anti-HAV) immunoglobulin M, hepatitis B surface antigen (HbsAg), and/or hepatitis C antibody (HCVAb);

e. Markers of hepatic inflammation or overt or occult cirrhosis as evidenced by one or more of the following:

1. Prothrombin time (PT) > upper limit of normal (ULN); prolonged international normalized ratio (INR) >ULN;

2. GLDH >2 x ULN;

3. Total bilirubin >1.5 x ULN (unless the participant has a history of Gilbert disease) and direct bilirubin >0.5 mg/dL;

4. Gamma-glutamyl transferase (GGT) >1.5 x ULN.

9. Other acute or chronic medical or psychiatric condition at Screening (Visit 1), including recent (within the past year) or active suicidal ideation or behavior (using screening by the Child Behavior Check List (CBCL) and determined by the Investigator, as described in Section 8.2.13) or laboratory abnormality that may increase the risk associated with study participation or IP administration or may interfere with the interpretation of study results and, in the judgment of the Investigator, would make the participant inappropriate for entry into this study.

10. Acute infection at Screening (Visit 1) or Baseline (Visit 2) that, in the judgement of the Investigator is not expected to be fully resolved at least 2 weeks before Day 1 (Visit 3). At Day 1 (Visit 3), participants must have been infection-free for at least 2 weeks prior to IP administration. Delay of IP administration for up to 14 days is permitted to enable infections to become fully resolved.

11. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the Investigator, or Pfizer employees, including their family members, directly involved in the conduct of the study.

12. Known hypersensitivity to any of the components of the IP or solution for infusion, such as hypersensitivity to albumin or a diagnosis of HFI. Symptoms suggestive of HFI include nausea, vomiting, bloating, stomach cramps, or diarrhea following the ingestion of sweet foods or drinks, or a pattern of avoiding sweet foods or drinks.

13. Contraindication to the use of eculizumab, as per the local prescribing information.

14. LVEF <50% on echocardiogram performed at the Screening Visit (Visit 1), as evaluated by the central reader.

15. Participants with the following genetic abnormalities in the dystrophin gene as confirmed by the investigator based on the review of DMD genetic testing:

    a. Any mutation (exon deletion, exon duplication, insertion, or point mutation) affecting any exon between exon 9 and exon 13, inclusive; OR

    b. A deletion that affects both exon 29 and exon 30;OR

    c. A deletion that affects any exons between 56-71, inclusive.

For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12.

16. Cardiac pathologies, as evaluated by a pediatric cardiologist at the Screening Visit (Visit 1):

    a. Diagnosis of myocarditis (eg, viral): either based on prior medical history or based on findings in cardiac imaging tests;

    b. Any other cardiac history, and/or condition and/or abnormalities in cardiac imaging, that determine that the participant should not be included in the study, as per the cardiologist.

17. Not a candidate for mechanical cardiac or respiratory support, or any other invasive intervention, if indicated for management of an acute event as determined by the cardiologist in consultation with the investigator at the Screening Visit (Visit 1).

10.15. Appendix 15: Russia Appendix

10.15.1. Schedule of Activities – Year 1

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [ss]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Informed consent/assent	X																						
Inform caregivers about study C3391007[dd]	X																						
Demography	X																						
Medical history	X[ii]																						
Medication history	X																						
Review of inclusion/exclusion criteria	X	X																					
Eligibility for Year 1 IP administration[v]			X																				
Hospital stay[jj]			X	→	→	→	→	X															
Physical examination[h]	X	X	X	X	X		X		X	X			X			X			X	X		X	X
Neurological examination[h]	X	X			X		X		X	X			X			X			X	X		X	X
Weight		X											X						X	X	X	X	X
Height	X												X						X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X			X			X	X		X	X
12-Lead ECG[k]	X		X				X			X												X	X
CBCL	X																					X	X[g]
Randomization		X[bb]																					
Laboratory Assessments[l]																							
Blood Samples																							
NAb	X	(X)[cc]											X									X	X[g]
ADA to mini-dystrophin and AAV9	X									X[ff]	X[ff]	X[ff]	X						X			X	X[g]
ELISpot to mini-dystrophin and AAV9		X														X							X[g]
Viral Vector Shedding[z]	X			X	X						X					X		X	X	X		X	X[g]
Clinical safety (hematology, other)[l]	X			X	X					X	X		X			X		X	X	X		X	X[g]

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Chemistry and hepatic safety [l]	X			X	X					X	X	X[ee]	X		X	X	X	X	X	X		X	X
Post IP intensified safety monitoring [l] [w]				X	X					X	X		X										
Local and central laboratory testing[aa]	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	
Cardiac Troponin I	X										X	X	X	X	X	X	X	X	X			X	X
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																					X	
Biomarker (creatine kinase)[l]		X			X					X	X	X	X		X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[m]	X																			X		X	

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Banked biospecimens for genetics[n]																		X					
Urine Samples																							
Clinical safety (urinalysis)[l]	X		X	X	X					X			X			X			X			X	X[g]
Banked biospecimens for biomarkers[m]	X																			X		X	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Saliva Samples																							
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Tissue Samples																							
Muscle biopsy[o]		X																				X[x]	
Imaging Assessments																							
Echocardiogram[p]	X																					X	X[g]
Cardiac MRI[gg]	X[hh]																					X[hh]	
Functional Assessments																							
FVC[q,y]	X																					X	X[g]
NSAA[q]	X	X														X			X	X		X	X

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Ankle range of motion	X	X														X			X	X		X	X
Ambulatory status	X[r]															X			X	X		X	X
Actigraphy[s]		X														X			X	X		X	
Clinical Outcome Assessments																							
Caregiver-completed																							
Modified PODCI – Pediatric Parent[t]		X																		X		X	X
EQ-5D-Y Proxy[t]		X																				X	X
EQ-5D-5L		X																				X	X
PGIS:CG[t]		X														X			X	X		X	X
Participant-completed																							
EQ-5D-Y[t]																						X	X
Clinical evaluator-completed																							
CGIS[q]		X														X			X	X		X	X
Health economic questionnaires																							
HRU:CG		X																					
WPAI:DMD Caregiver		X																					
Interventions																							
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X					

Period	Screening	Baseline	Main Study Period (Year 1)																				Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Background glucocorticoid regimen	X	X																X	→	→	→	→	
IP administration			X																				
Meningococcal vaccine	X	X																					
Ongoing monitoring																							
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate. Schedule of Activities – Year 2 and Long-Term Follow Up

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;
- Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:
- Schedule A:

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- **First day:** collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place the next day or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.

- Schedule B:
  - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).
- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;
- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;
- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);
- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

b. **Visit 14** and **Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a);

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- For sites outside the US, the Baseline visit should occur at least 31 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);
- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).
- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

l. **Clinical laboratory tests** are described in detail in Table 5 (Appendix 15).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings (with the potential to collect a maximum of 33 if needed), at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline Visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline Visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

x. All participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. See Section 8.8.5 for additional details.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 9 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details, please see Section 8.2.12 and Section 10.15.1.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2 weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details- please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. For US sites, only when approved by the relevant Institutional Review Board.

ee. On Day 28 (Visit 12.2), only GLDH will be collected.

ff. ADA to mini-dystrophin only.

gg. Investigators will discuss with the participant and/or their caregiver the importance of having a baseline cardiac MRI, even under general anesthesia, to be able to assess and manage potential cardiac adverse events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast

Period	Screening	Baseline	Main Study Period (Year 1)																			Early Discontinuation Visit [g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

hh. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

ii. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

jj. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

kk. This visit is for sites in Germany only. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

10.15.2. Schedule of Activities – Year 2 and Long Term Follow Up

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Eligibility for Year 2 IP administration[r]	X																					
Hospital stay[dd]	X	→	→	→	→	**X**																
Physical examination[g]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X			X			X	X	X	X	X	X
Height and Weight											X						X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X											X		X	X
CBCL																			X	X	X	X[e]
Laboratory Assessments[k]																						
Blood Samples																						
NAb to AAV9											X								X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X						X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X													X							X[w]	X[e]
Viral Vector Shedding[u]								X						X		X	X	X			X	X[e]
Clinical safety (hematology, other) [k]		X	X					X	X		X			X		X	X	X	X	X	X	X[e]

Period	**Year 2**																		**Long-term follow up**		**Early Discontinuation Visit [e]**
Visit Number/Description	**Visit 20[a,bb,cc]**	**Visit 21[bb, cc]**	**Visit 22[bb, cc]**	**Visit 23[bb, cc]**	**Visit 24[bb, cc]**	**Visit 25[bb,cc] &26 [bb, cc]**	**Visit 27[bb, cc]**	**Visit 28[bb, cc]**	**Visit 29[b,bb, cc]**	**Visit 29.2[b, bb, cc]**	**Visit 30[bb, cc]**	**Visit 30.1[cc, bb,cc]**	**Visit 30.2[b, bb, cc]**	**Visit 31[c,cc]**	**Visit 31.2[b,cc]**	**Visit 32[b,cc]**	**Visit 33**	**Visit 34**	**Visit 35**	**Visits 36, 38, 40, 42[d]**	**Visits 37, 39, 41, 43[d]**	
	Year 2, Week 1, Day 1	**Year 2, Week 1, Day 2**	**Year 2, Week 1, Day 4**	**Year 2, Week 1, Day 6**	**Year 2, Week 1, Day 7**	**Year 2, Week 2, Days 8 &9**	**Year 2, Week 2, Day 10**	**Year 2, Week 2, Day 14**	**Year 2, Week 3**	**Year 2, Week 4**	**Year 2, Week 5**	**Year 2, Week 6**	**Year 2, Week 7**	**Year 2, Week 9**	**Year 2, Week 11**	**Year 2, Week 13**	**Year 2, Week 18**	**Year 2, Week 35**	**Year 2, Week 52**	**Years 3, 4, 5, 6[d]**	**Years 3, 4, 5, 6[d]**	
Visit Day	**390**	**391**	**393**	**395**	**396**	**397& 398**	**399**	**403**	**410**	**417**	**423**	**431**	**437**	**449**	**463**	**479**	**509**	**629**	**749**	**930, 1290, 1650, 2010[d]**	**1110, 1470, 1830, 2190[d]**	
Visit Window (± days)	**3[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**2[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**3[f]**	**7[f]**	**7[f]**	**7[f]**	**30[f]**	**30[f]**	
Chemistry and hepatic safety[k]		X	X					X	X	X[y]	X		X	X	X	X	X	X	X	X	X	
Post IP intensified safety monitoring[k,s]		X	X					X	X		X											
Local and central laboratory testing[x]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Cardiac Troponin I									X	X	X	X	X	X	X	X	X		X	X	X	X
Biomarker (creatine kinase)[k]			X					X	X	X	X		X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																		X	X			
Urine Samples																						
Clinical safety (urinalysis)[k]	X	X	X						X	X		X		X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																		X	X			
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Saliva Samples																						
Viral Vector Shedding[u]						X				X				X		X	X	X	X		X	X[e]
Tissue Sample																						
Muscle Biopsy																					X[ff]	
Imaging Assessments																						
Echocardiogram[m]																			X		X	X[e]

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Cardiac MRI[aa]																			X[aa]			
Functional Assessments																						
FVC[n,t]																			X		X	X[e]
NSAA[n]														X			X	X	X	X	X	X
Ankle range of motion														X			X	X	X	X	X	X
Ambulatory status														X			X	X	X	X	X	X
Actigraphy[o]														X			X	X	X	X	X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI – Pediatric Parent[p]																		X	X	X	X	X
EQ-5D-Y Proxy[p]																			X		X	X
EQ-5D-5L																			X		X	X
PGIS:CG[p]														X			X	X	X	X	X	X
Participant-completed																						
Modified PODCI – Adolescent[p]																				X	X	X
EQ-5D-Y[p]																			X		X	X
PGIS[p]																				X	X	X
Clinical evaluator-completed																						
CGIS[n]														X			X	X	X	X	X	X
Health economic questionnaires																						
HRU:CG																			X		X	X

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
WPAI:DMD Caregiver																			X		X	X
Study Interventions																						
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X						
Background glucocorticoid regimen																X	→	→	→	X[v]	X[v]	
IP administration	X																					
Ongoing monitoring																						
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5 Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. **Visit 20 – Year 2, Week 1, Day 1**

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);
- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed **prior to IP administration**: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.
- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel, see Appendix 16 .

b. **Visits 29, 29.2, 30.2, 31.2, and 32**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

c. **Visit 31** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. **Visit 42 and 43 – Long-term follow up Year 6**

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. **Early Discontinuation Visit**

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

f. **Visit Windows for Visits 20 through Visit 43**

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief **physical and neurological examinations,** as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

h. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

j. **12 Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. **Clinical laboratory tests** are described in detail in in Table 5 (Section 10.15.1).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

m. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

n. The **NSAA** and **CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. **An activity monitor** may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

p. **COAs** will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 bb, cc	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[cc, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26 and 27. For more details please see Section 8.2.12 and Appendix 15.

y. On Day 417 (Visit 29.2), only GLDH will be collected.

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] &26 [bb, cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b,bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

ee. This visit is for sites in Germany only. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ff. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

10.15.3. Clinical Laboratory Tests

The following safety laboratory tests will be performed at times defined in Sections 10.15.1 and 10.15.2 of this protocol. Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory; or as derived from calculated values. These additional tests would not require additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety concerns.

Table 5. Protocol Required Safety Laboratory Assessments in Russia

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[a]	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		

Table 5. Protocol Required Safety Laboratory Assessments in Russia

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] Urine biomarkers
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
Local assessment of NT-ProBNP/BNP, if needed as per Section 8.2.7

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 CO^2 (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

Table 5. Protocol Required Safety Laboratory Assessments in Russia

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 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
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

Table 5. Protocol Required Safety Laboratory Assessments in Russia

Central Laboratory	
Clinical safety	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 393 (Visits 21 and 22) in Year 2
Chemistry and hepatic safety	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 393 (Visits 21 and 22) in Year 2
Urinalysis	Days 2 and 4 (Visits 4 and 5) in Year 1 Days 391 and 393 (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 he/she 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.

Any remaining biospecimens samples collected for clinical safety be retained and stored for the duration of the study. Retained samples may be used for the assessment of exploratory biomarkers. These data will not be included in the clinical study report.

Investigators must document their review of each laboratory safety report.

10.16. Appendix 16: Israel Appendix

10.16.1. Schedule of Activities – Year 1 (Screening to Year 1 Day 360)

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	
Informed consent/assent	X																						
Inform caregivers about study C3391007[dd]	X																						
Demography	X																						
Medical history	X[ii]																						
Medication history	X																						
Review of inclusion/exclusion criteria	X	X																					
Eligibility for Year 1 IP administration[v]			X																				
Hospital stay[jj]			X	→	→	→	→	X															
Physical examination[h]	X	X	X	X	X		X		X	X			X			X			X	X		X	X
Neurological examination[h]	X	X			X		X		X	X			X			X			X	X		X	X
Weight		X											X						X	X	X	X	X
Height	X												X						X	X		X	X

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Vital signs (supine BP, respiratory rate, PR, body temp, and O2 saturation)[i,j]	X	X	X	X	X	X	X	X	X	X			X			X			X	X		X	X
12-Lead ECG[k]	X		X				X			X												X	X
CBCL	X																					X	X[g]
Randomization		X[bb]																					
Laboratory Assessments[l]																							
Blood Samples																							
NAb	X	(X)[cc]											X									X	X[g]
ADA to mini-dystrophin and AAV9	X									X[ff]	X[ff]	X[ff]	X						X			X	X[g]
ELISpot to mini-dystrophin and AAV9		X														X							X[g]
Viral Vector Shedding[z]	X			X	X						X					X		X	X	X		X	X[g]
Clinical safety (hematology, other)[l]	X			X	X					X	X		X			X		X	X	X		X	X[g]
Chemistry and hepatic safety [l]	X			X	X					X	X	X[ee]	X		X	X	X	X	X	X		X	X

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Post IP intensified safety monitoring[l,w]				X	X					X	X		X										
Local and central laboratory testing[aa]	X[ll]	X		X	X	X	X	X	X	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]	X[ll]		X[ll]	
Cardiac Troponin I	X										X	X	X	X	X	X	X	X	X			X	X
International normalized ratio (INR), Hepatitis A virus (anti-HAV) immunoglobulin M Hepatitis B surface antigen, Hepatitis C antibody[l]	X																					X	
Biomarker (creatine kinase)[l]		X			X					X	X	X	X		X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[m]	X																			X		X	
Banked biospecimens for genetics[n]																		X					
Urine Samples																							

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Clinical safety (urinalysis)[l]	X		X	X	X					X			X			X			X			X	X[g]
Banked biospecimens for biomarkers[m]	X																			X		X	
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Saliva Samples																							
Viral Vector Shedding[z]	X		X	X	X		X		X	X	X		X			X		X	X	X		X	X[g]
Tissue Samples																							
Muscle biopsy[o]		X																				Xx	
Imaging Assessments																							
Echocardiogram[p]	X																					X	X[g]
Cardiac MRI[gg]	X[hh]																					X[hh]	
Functional Assessments																							
FVC[q, y]	X																					X	X[g]
NSAA[q]	X	X														X			X	X		X	X
Ankle range of motion	X	X														X			X	X		X	X
Ambulatory status	X[r]															X			X	X		X	X
Actigraphy[s]		X														X			X	X		X	
Clinical Outcome Assessments																							

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Caregiver-completed																							
Modified PODCI – Pediatric Parent[t]		X																		X		X	X
EQ-5D-Y Proxy[t]		X																				X	X
EQ-5D-5L		X																				X	X
PGIS:CG[t]		X														X			X	X		X	X
Participant-completed																							
EQ-5D-Y[t]																						X	X
Clinical evaluator-completed																							
CGIS[q]		X														X			X	X		X	X
Health economic questionnaires																							
HRU:CG		X																					
WPAI:DMD Caregiver		X																					
Interventions																							
Protocol-mandated glucocorticoid regimen[u]			X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X					
Background glucocorticoid regimen	X	X																X	→	→	→	→	
IP administration			X																				
Meningococcal vaccine	X	X																					
Ongoing monitoring																							

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	**Visit 1[a]**	**Visit 2[c]**	**Visit 3[d]**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**	**Visits 8 & 9**	**Visit 10**	**Visit 11**	**Visit 12[e]**	**Visit 12.2[e]**	**Visit 13**	**Visit 13.1[kk]**	**Visit 13.2[e]**	**Visit 14[b]**	**Visit 14.2[e]**	**Visit 15[e]**	**Visit 16**	**Visit 17**	**Visit 18[f]**	**Visit 19[b]**	
	Screening	**Baseline**	**Week 1, Day 1**	**Week 1, Day 2**	**Week 1, Day 4**	**Week 1, Day 6**	**Week 1, Day 7**	**Week 2, Day 8 & 9**	**Week 2, Day 10**	**Week 2, Day 14**	**Week 3**	**Week 4**	**Week 5**	**Week 6**	**Week 7**	**Week 9**	**Week 11**	**Week 13**	**Week 18**	**Week 35**	**Week 47**	**Week 52**	
Visit Day	**-90 to -30**	**-48 to -16**	**1**	**2**	**4**	**6**	**7**	**8 & 9**	**10**	**14**	**21**	**28**	**34**	**42**	**48**	**60**	**74**	**90**	**120**	**240**	**328**	**360**	
Visit Window (± days)			**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**1**	**1**	**3**	**3**	**3**	**3**	**3**	**7**	**7**	**14**	**7**	
Concomitant medications	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	X	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9=adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG=electrocardiogram; ELISpot=Enzyme-Linked ImmunoSpot; EQ-5D-Y=EuroQol 5 Dimensions–Youth; FVC=Forced Vital Capacity; IP=investigational product; Men ACWY=Meningococcal serogroups A, C, W, and Y; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS=patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; temp=temperature; PR=pulse rate. Schedule of Activities – Year 2 and Long-Term Follow Up

a. **Visit 1 – Screening Visit**

- During screening, participants and caregiver(s) will be assessed for study eligibility in accordance with the Inclusion/Exclusion Criteria as described in Section 5.1 and Section 5.2;
- Visit 1 must be conducted over the course of 2 days. The investigator will decide which of the schedules below they will follow and inform the study team:
- Schedule A:
    - **First day:** collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding. **Second day**: should take place the next day or as soon as possible, after the first day: clinical safety (See Appendix 2), INR, cardiac troponin I.
- Schedule B:
    - **First day**: collection of blood, urine and saliva for anti-HAV immunoglobulin M, hepatitis B surface antigen, hepatitis C antibody, NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers and viral vector shedding. **Second day**: must take place only when the results of the test for NAb to AAV9 are available. The time between the first and second day of the Screening Visit is expected to be between 3-4 weeks (based on the time to obtain the results of the NAb to AAV9 test). Only participants with a negative test for NAb to AAV9 will perform the rest of the Visit 1 assessments as per

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

SoA. This includes the collection of blood and urine for: clinical safety tests (see Appendix 2), INR and cardiac troponin I. Participants with a positive test for NAb to AAV9 will be screen failed and will not attend the second day of Screening Visit (Visit 1).

- Informed consent must be provided by the caregiver(s). The participant may also be required to provide assent in compliance with local regulations and institutional review board (IRB) requirements;
- Screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition may be repeated once during the screening period for confirmation of eligibility;
- Demographics: Information such as date of birth, race and ethnicity and gender will be collected in compliance with local regulations;
- Medical history will include results of genetic testing for confirmation of diagnosis of DMD. Results must confirm the presence of an abnormality (eg, deletion, duplication), or a point mutation in the dystrophin gene(s) which is consistent with the diagnosis of DMD. The mutation type will be reported. If the Investigator determines that the results are inconclusive, a repeat genetic testing will be allowed through the central laboratory at Screening (Visit 1) prior to any other assessments. In that case participants may return for the remainder of Screening (Visit 1) once results are confirmed (Section 8.7.1);
- Medical history will also be reviewed for any significant medical history and concurrent illness(es) that required or are requiring specialist consultation or treatment;
- Medication history: Complete medication history will include all prescription or nonprescription drugs, and dietary and herbal supplements taken within 30 days prior to the Screening Visit (Visit 1). The date the participant first started glucocorticoids for their DMD and the date of start of the background glucocorticoid regimen that the participant is taking at the time of Visit 1 (Screening Visit) must also be documented. In addition, the general immunization status including the immunization status against meningococcus, and any other vaccine(s) required by the eculizumab local prescribing information, must be documented;
- Meningococcal vaccine: Participants who have no contraindications and who have not previously received a MenACWY vaccination; or whose last vaccination at the time of the Screening Visit (Visit 1) is outside the time period of active coverage specified by the vaccine manufacturer (Visit 1) must receive at least one dose of MenACWY vaccine as early as possible in the Screening Period and not later than 30 days before IP administration (see Section 6.5.1). Participants must also receive MenB vaccination if indicated by national vaccination guidelines. In addition, local eculizumab prescribing information, including additional vaccination and other requirements must also be followed (see Section 6.5.1).
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6).

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

b. **Visit 14** and **Visit 19** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory samples must be collected:

Visit 14 (Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

Visit 19 (Week 52)

First day: anti-HAV immunoglobulin M, Hepatitis B surface antigen, Hepatitis C antibody (these tests will not be applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 [see Section 5.2]), NAb to AAV9, ADA to mini-dystrophin and AAV9, banked biospecimens for biomarkers, viral vector shedding.

Second day: clinical safety, INR, cardiac troponin I, biomarker (creatine kinase).

c. **Visit 2 – Baseline Visit**

- Meningococcal vaccine: Only applicable for participants who have not received this vaccination at Screening (please refer to footnote a);
- For sites outside the US, the Baseline visit should occur at least 31 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team. For US sites the Baseline visit should occur at least 16 calendar days prior to the planned IP administration visit, Day 1 (Visit 3), to allow for timely delivery of IP to the site, unless notified of earlier or later IP delivery by the study team;
- IP will be shipped to site following confirmation of participant's eligibility (Section 5.1 and Section 5.2) and randomization. The amount of IP to be shipped to the site for IP administration at Visit 3 will be based on the measurement of body weight at the Baseline Visit (Visit 2). Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site.
- Unplanned Visit: If the 90-day period between screening and dosing is exceeded due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to re-confirm study/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments (see Sections 5.3 and 5.6)

d. **Visit 3 – Week 1, Day 1 (Day of IP administration)**

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- Prior to IP administration, the Investigator must confirm applicable IP eligibility criteria (Section 6.1.1);
- Participants will be instructed not to take their background glucocorticoid dose on Day 1 (Visit 3);
- Participants are to be admitted to the site;
- The following assessments must be performed **prior to IP administration**: physical examination, urine sample collection, ECG and vital signs;
- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes to +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site to enable prompt follow-up in the event of any emergent AEs through Day 14 (Visit 11), or longer if deemed necessary.

e. **Visits 12, 12.2, 13.2, 14.2 and 15**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

f. **Visit 18**

- This visit may be performed remotely (at or close to the participant's home); in that case, it should include phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.
- Amount of IP to be shipped to site for the IP administration on Day 390 (Visit 20) will be based on the measurement of body weight obtained at this visit. Body weight measurement must be verified by two site personnel and entered into the interactive response technology drug management system to trigger IP shipment to the site. This visit is not applicable for Cohort 1 participants confirmed to meet exclusion criterion 15 (see Section 5.2).

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

- For participants who undergo Day 328 (Visit 18) during a study dosing pause, the amount of IP to be shipped to the site will be determined once the study has been restarted. Therefore, the weight collected at Day 328 (Visit 18) will not be entered into the interactive response technology drug management system during the dosing pause. Participants will be evaluated for Year 2 IP eligibility when the study is restarted.
- May not be applicable for participants confirmed to meet exclusion criterion 15 or those who declined Year 2 IP administration (see Appendix 12 and Section 7.2.1).

g. **Early Discontinuation Visit**

- This visit is not applicable for participants who withdraw prior to Day 1 (Visit 3) or for Cohort 2 participants who are withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7.1).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only if the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.
- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

h. **Brief physical and neurological examinations**, as described in Section 8.2, are acceptable post-baseline unless safety concerns warrant full examination.

i. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

j. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

k. **12-Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

l. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

- For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.
- On the following visits: Baseline Visit (Visit 2), Day 60 (Visit 14), Day 120 (Visit 16), Day 240 (Visit 17) and Day 360 (Visit 19), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

m. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

n. **Banked biospecimens for genetics** are collected as described in Section 8.7.2.

o. **Open muscle biopsies** will be obtained in approximately the first 15 participants randomized into Cohorts 1 and 2, and their siblings (with the potential to collect a maximum of 33 if needed), at sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies, following administration of an anesthetic (eg, regional block or under general anesthesia) according to institutional standard practice, and only after any imaging and functional assessments scheduled for the same visit have been completed. Baseline Visit muscle biopsies will be performed after randomization. If a muscle biopsy cannot be scheduled on the day of the Baseline Visit, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing.

p. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

q. The **NSAA and CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, ankle range of motion and FVC may be video recorded at the Day 1 (Screening Visit), Baseline Visit (Visit 2), and at the annual visits (ie, Visits 19, 35, 37, 39, 41, 43). If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

r. **Ambulatory assessment** at Screening (Visit 1) is based only on the ability to perform the 10 m run/walk, as assessed during the NSAA.

s. **An activity monitor** will be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

t. **COAs** will be completed by the caregiver on behalf of the participant and/or by the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

u. Starting on Day 1 (Visit 3) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1).

v. For eligibility for Year 1 IP administration please see Section 6.1.1.

w. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

x. All participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo 2 post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-baseline muscle biopsy cannot be performed on the scheduled day, the biopsy may be performed at a later day, as long as it is at least 2 weeks before dosing for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

y. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

z. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) only after IP administration, as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix. See Section 8.8.5 for additional details.

aa. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 9 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 6, 7, 8, 9, and 10. For more details, please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 4 and 5, see Appendix 2 for details.

bb. In order to ensure an adequate understanding and management of potential safety risks, the initial rate of randomization into the study will be limited. No more than 2 participants per week will be randomized at the start of the study, until 4 participants have been observed for at least 2 weeks post IP administration. After that, the rate could be increased to no more than 3 participants randomized per week (until at total of 10 participants have been observed for at least 2 weeks post-IP administration). Thereafter, the rate of randomization could be further increased to no more than 5 participants randomized per week (until a total of 20 participants have been observed for at least 2

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

weeks post-IP administration). After this time, no limits of the randomization rate will be imposed unless the study team, in consultation with the E-DMC, determines otherwise. For more details- please see Section 4.1.

cc. The NAb to AAV9 blood samples at the Baseline Visit (Visit 2) will always be collected and sent to the Central Laboratory, but will only be analyzed and reviewed prior to Day 1 Visit (Visit 3) if the time between the first blood draw for NAb to AAV9 testing at the Screening Visit (Visit 1) or most recent test, if repeat blood draw(s) was required, and the Day 1 Visit (Visit 3) is expected to be more than 55 days, which is anticipated to occur rarely. Dosing cannot occur unless there is a negative test to AAV9 from a sample collected 55 or less days before the day of IP administration.

dd. For US sites, only when approved by the relevant Institutional Review Board.

ee. On Day 28 (Visit 12.2), only GLDH will be collected.

ff. ADA to mini-dystrophin only.

gg. Investigators will discuss with the participant and/or their caregiver the importance of having a baseline cardiac MRI, even under general anesthesia, to be able to assess and manage potential cardiac adverse events during the study. This discussion and the decision to perform or not a baseline cardiac MRI will be documented in the participant's records. A participant requiring anesthesia or unable to undergo investigation with closed MRI (eg, metal implants) may be exempt, and will be allowed to be randomized in the study without a cardiac MRI. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8).

hh. Cardiac MRI may be performed at any time between the first day of the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), and after randomization, as long as it is done before Day 1 (Visit 3). If a prior cardiac MRI was performed within 6 months of the Screening Visit (with gadolinium, or without gadolinium if contrast administration is contraindicated), and results are available, then a cardiac MRI at screening will not be performed. Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

ii. Participants will be assessed by a cardiologist at the Screening Visit, see Section 5.2, exclusion criteria 16 and 17.

jj. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 8, or later if deemed necessary by the Investigator (see Section 8.2.10).

Period	Screening	Baseline		Main Study Period (Year 1)																		Early Discontinuation Visit[g]
Visit Number/ Description	Visit 1[a]	Visit 2[c]	Visit 3[d]	Visit 4	Visit 5	Visit 6	Visit 7	Visits 8 & 9	Visit 10	Visit 11	Visit 12[e]	Visit 12.2[e]	Visit 13	Visit 13.1[kk]	Visit 13.2[e]	Visit 14[b]	Visit 14.2[e]	Visit 15[e]	Visit 16	Visit 17	Visit 18[f]	Visit 19[b]	
	Screening	Baseline	Week 1, Day 1	Week 1, Day 2	Week 1, Day 4	Week 1, Day 6	Week 1, Day 7	Week 2, Day 8 & 9	Week 2, Day 10	Week 2, Day 14	Week 3	Week 4	Week 5	Week 6	Week 7	Week 9	Week 11	Week 13	Week 18	Week 35	Week 47	Week 52	
Visit Day	-90 to -30	-48 to -16	1	2	4	6	7	8 & 9	10	14	21	28	34	42	48	60	74	90	120	240	328	360	
Visit Window (± days)			0	0	0	0	0	0	0	1	1	1	1	3	3	3	3	3	7	7	14	7	

kk. This visit is for sites in Germany only and only to test cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ll. Only for sites in Russia

10.16.2. Schedule of Activities – Year 2 and Long Term Follow Up

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Eligibility for Year 2 IP administration[r]	X																					
Hospital stay[dd]	X	→	→	→	→	X																
Physical examination[g]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
Neurological examination[g]			X		X		X	X			X			X			X	X	X	X	X	X
Height and Weight											X						X	X	X	X	X	X
Vital signs (supine BP, respiration, PR, body temp, and O2 saturation)[h,i]	X	X	X		X		X	X			X			X			X	X	X	X	X	X
12-Lead ECG[j]	X				X			X											X		X	X
CBCL																			X	X	X	X[e]
Laboratory Assessments[k]																						
Blood Samples																						
NAb to AAV9											X								X		X	X[e]
ADA to mini-dystrophin and AAV9								X[z]	X[z]	X[z]	X						X		X		X	X[e]
ELISpot to mini-dystrophin and AAV9	X													X							X[w]	X[e]
Viral Vector Shedding[u]								X						X		X	X	X			X	X[e]
Clinical safety (hematology, other)[k]		X	X					X	X		X			X		X	X	X	X	X	X	X[e]

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Chemistry and hepatic safety[k]		X	X					X	X	X[y]	X		X	X	X	X	X	X	X	X	X	
Post IP intensified safety monitoring[k,s]		X	X					X	X		X											
Local and central laboratory testing[x]	X	X	X	X	X	X	X	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]	X[gg]				
Cardiac Troponin I									X	X	X	X	X	X	X	X	X		X	X	X	X
Biomarker (creatine kinase)[k]			X					X	X	X	X		X	X	X	X	X	X	X		X	X
Banked biospecimens for biomarkers[l]																		X	X			
Urine Samples																						
Clinical safety (urinalysis)[k]	X	X	X					X	X		X			X			X		X		X	X[e]
Banked biospecimens for biomarkers[l]																		X	X			
Viral Vector Shedding[u]					X				X					X		X	X	X	X		X	X[e]
Saliva Samples																						
Viral Vector Shedding[u]						X				X				X		X	X	X	X		X	X[e]
Tissue Sample																						
Muscle Biopsy																					X[ff]	
Imaging Assessments																						
Echocardiogram[m]																			X		X	X[e]
Cardiac MRI[aa]																			X[aa]			

Period	Year 2																		Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Functional Assessments																						
FVC[n,t]																			X		X	X[e]
NSAA[n]														X			X	X	X	X	X	X
Ankle range of motion														X			X	X	X	X	X	X
Ambulatory status														X			X	X	X	X	X	X
Actigraphy[o]														X			X	X	X	X	X	
Clinical Outcome Assessments																						
Caregiver-completed																						
Modified PODCI – Pediatric Parent[p]																		X	X	X	X	X
EQ-5D-Y Proxy[p]																			X		X	X
EQ-5D-5L																			X		X	X
PGIS:CG[p]														X			X	X	X	X	X	X
Participant-completed																						
Modified PODCI – Adolescent[p]																				X	X	X
EQ-5D-Y[p]																			X		X	X
PGIS[p]																				X	X	X
Clinical evaluator-completed																						
CGIS[n]														X			X	X	X	X	X	X
Health economic questionnaires																						
HRU:CG																			X		X	X
WPAI:DMD Caregiver																			X		X	X

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	
Study Interventions																						
Protocol-mandated glucocorticoid regimen[q]	X	X	→	→	→	→	→	→	→	→	→	→	→	→	→	X						
Background glucocorticoid regimen																X	→	→	→	X[v]	X[v]	
IP administration	X																					
Ongoing monitoring																						
Concomitant medications	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X
Serious and nonserious adverse event monitoring	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X

Abbreviations/Acronyms: →=continuous monitoring/event; AAV9= adeno associated virus serotype 9; ADA=anti-drug antibody; BP=Blood pressure; CG=Caregiver; CGIS=Clinician Global Impression of Severity; CBCL=Child Behavior Check List; ECG = electrocardiogram; ELISpot= Enzyme-Linked ImmunoSpot; EQ-5D-Y= EuroQol 5 Dimensions–Youth; FVC= Forced Vital Capacity; IP=investigational product; NAb=neutralizing antibodies; NSAA=North Star Ambulatory Assessment; PGIS= patient global impression of severity; PODCI=Pediatric Outcomes Data Collection Instrument; PR=pulse rate; temp=temperature.

a. **Visit 20 – Year 2, Week 1, Day 1**

- Prior to IP administration, the Investigator must confirm applicable Year 2 IP administration eligibility criteria (Section 7.1);
- Participants are to be admitted to the site;
- Participants will be instructed not to take their background glucocorticoid dose on Day 390 (Visit 20);
- The following assessments must be performed **prior to IP administration**: Physical examination, blood collection (ELISpot to mini-dystrophin and AAV9), urine sample collection, ECG and vital signs;

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- Participants will receive an intravenous infusion of 2 mg/kg of methylprednisolone approximately **1 to 4 hours prior to infusion of IP**;
- IP administration over approximately 2 to 4 hours (-15 minutes or +30 minutes including flush);
- Vital signs will be monitored at approximately 30 minutes, 1, 2, 4, 8, and 10 hours after start of infusion, and 3 times per day after that for the duration of the hospital stay. Participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).
- If adverse events (AEs) possibly related to IP administration are observed, participants should not be discharged until the events have resolved. Upon discharge, participants should stay near the site for at least 7 additional days to enable prompt follow-up in the event of any emergent AEs through Day 403 (Visit 28), or longer if deemed necessary.
- If the time between the blood draw for the clinical safety laboratory tests on Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) exceeds 13 weeks (90 days), due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP. The participant will not be withdrawn due to exceeding the time between Day 360 Visit (Visit 19) and Day 390 Visit (Visit 20), as described in Section 7.1.
- If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), a participant's Year 2 IP administration must be delayed, the Day 390 (Visit 20) and also subsequent visits will be delayed for that participant until the pause is lifted. If the pause is not lifted within 6 months of the Day 360 (Visit 19), the participant will undergo an unplanned visit for general monitoring on Day 540 ±7 days, and approximately every 6 months afterwards until the pause is lifted (or more frequently if considered necessary by the investigator) for sites in Israel.

b. **Visits 29, 29.2, 30.2, 31.2, and 32**

- Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

c. **Visit 31** must be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, the follow-up day visit, on the second day, to complete blood collection, may be performed remotely, to allow blood collection at or close to the participant's home. The following laboratory assessments must be collected as follows:

Visit 31 (Year 2, Week 9)

First day: ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

d. **Visit 42 and 43 – Long-term follow up Year 6**

- All participants will be followed for 5 years after receiving fordadistrogene movaparvovec. Therefore Visits 42 and 43 only apply to participants randomized to Cohort 2.

e. **Early Discontinuation Visit**

- This visit is not applicable for Cohort 2 participants who were withdrawn from the study between Day 360 (Visit 19) and Day 390 (Visit 20) (see Section 7).
- The site will contact the Sponsor to determine which laboratory (blood) tests should be collected at the Early Discontinuation Visit, to ensure that the daily and 4-week maximum blood volume limits are not exceeded.
- CBCL questionnaire: Only if the previous CBCL questionnaire was completed more than 2 months before the date of the Early Discontinuation Visit.
- NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9: Only if the participant discontinues the study before Visit 37 (Year 3, Day 1110).
- Clinical Safety: Only if the previous analysis had been done more than 1 month before the date of the Early Discontinuation visit.
- Echocardiogram: Only if the previous echocardiogram had been done more than 6 months before the date of the Early Discontinuation Visit.
- FVC: Only If the previous FVC had been assessed more than 2 months before the date of the Early Discontinuation Visit.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

- Viral vector shedding: For any given matrix, if the sample(s) had still being collected at the participant´s last study visit, it should also be collected at the Early Discontinuation Visit.

f. **Visit Windows for Visits 20 through Visit 43**

- The number of days between each visit for Visit 20 (Year 2, IP administration) through Visit 43 must be maintained irrespective of the actual visit day of Visit 20, eg, if the actual visit day at Visit 20 is 392 (instead of 390), then Visit 21 will take place on Day 393 (instead of Day 391), etc.

g. Brief **physical and neurological examinations,** as described in Section 8.2, are acceptable unless safety concerns warrant full examination.

h. **O2 saturation** will only be measured before the start of the IP infusion and during the inpatient stay post IP administration.

i. **Vital signs** will be measured 3 times per day during the inpatient stay post IP administration.

j. **12 Lead ECG** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

k. **Clinical laboratory tests** are described in detail in Table 3 (Appendix 2).

For urinalysis, a microscopic analysis will be performed only if urine dipstick is positive for blood, protein, nitrites or leukocyte esterase.

If the time between the blood draw for the clinical safety laboratory tests on Visit 19 (Day 360) and the planned Visit 20 (Day 390) exceeds 13 weeks (90 days due to operational or administrative reasons [eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays]), then the clinical safety laboratory tests should be repeated and eligibility (re)confirmed prior to administering IP, but the participant will not be withdrawn due to exceeding the time between Visit 19 (Day 360) and the planned Visit 20 (Day 390), as described in Section 7.1.

l. **Banked biospecimens for biomarkers** are collected as described in Section 8.8.4.

m. **Echocardiograms** will be collected and read locally for immediate interpretation and safety monitoring and will be submitted to a central laboratory for standardized interpretation.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

n. The **NSAA** and **CGIS** will be administered by a single clinical evaluator at each visit and whenever possible, the same CE should administer the functional assessments (NSAA, ankle range of motion and FVC) for the same participant throughout the study. The NSAA, range of motion and FVC may be video recorded at the annual visits. If CE re-training is required, the assigned master physiotherapist may request additional visits to be recorded and reviewed. Whenever possible, motor functional assessments should be performed early in the course of the visit, to help reduce the effect of fatigue on the participants´ performance; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual. On the following visits: Day 449 (Visit 31), Day 509 (Visit 33), Day 629 (Visit 34) and Day 749 (Visit 35), in which functional assessments (eg, NSAA) are performed, blood draws should always be done first, whenever possible, to ensure that the CK levels are obtained prior to the functional test; for additional advice regarding the ordering of assessments please consult the Functional Assessment Manual.

o. **An activity monitor** may be placed on the participant's ankle prior to the performing of other functional assessments and is to be worn continuously for the subsequent 2 weeks.

p. **COAs** will be completed by the caregiver on behalf of the participant and/or the participants themselves, depending on the participant's age and at the discretion of the Investigator and caregiver, as described in Section 8.1.7.

q. Starting on Day 390 (Visit 20) participants will not take their background **glucocorticoid regimen**. Participants will replace their background glucocorticoid regimen with the protocol-mandated glucocorticoid regimen for 90 days post-IP administration, after which, as long as there is no immune response or other clinical indication, participants may return to their background glucocorticoid regimen (see Section 6.5.1). If, due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays), participants must delay Year 2 IP administration, they will not receive the protocol-mandated glucocorticoid regimen until the pause is lifted and Year 2 IP administration takes place; they will remain on their background glucocorticoid regimen until then.

r. For eligibility for Year 2 IP administration please see Section 7.1.

s. For details regarding post IP intensified safety monitoring please see Section 8.2.10.

t. FVC will be assessed throughout the study on participants who are ≥6 years old at Screening. Participants <6 years old at the Screening Visit (Visit 1) will not have FVC evaluated at any time during the study.

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb,cc]	Visit 21[bb,cc]	Visit 22[bb,cc]	Visit 23[bb,cc]	Visit 24[bb,cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb,cc]	Visit 28[bb,cc]	Visit 29[b,bb,cc]	Visit 29.2[b,bb,cc]	Visit 30[bb,cc]	Visit 30.1[ee,bb,cc]	Visit 30.2[b,bb,cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

u. Viral vector shedding will be measured in approximately the first 45 treated participants (approximately 30 treated with fordadistrogene movaparvovec and approximately 15 treated with placebo) as described in Section 8.8.5. For each of the approximately 45 first treated participants, sample collection for a particular matrix (sample type) will be stopped when at least 2 consecutive negative results are observed in that matrix.

v. After two years (Day 749), any change to the background glucocorticoid regimen will be permitted (see Section 6.5.1).

w. ELISpot to mini-dystrophin and AAV9 if a clinical event has occurred that, in the opinion of the Sponsor and/or the Investigator, could be due to an immunological reaction. If ELISpot is to be collected, these visits should be conducted in the course of two (preferably consecutive) days in order to comply with daily blood volume limits. The following laboratory assessments must be collected as follows:

First day: NAb to AAV9, ADA to mini-dystrophin and AAV9, ELISpot to mini-dystrophin and AAV9, viral vector shedding.

Second day: clinical safety, cardiac troponin I, biomarker (creatine kinase).

x. Urine and some blood samples will be collected for local laboratory testing to ensure fast turnaround of test results. Some blood samples ie, GLDH at Visit 26 will be sent to the central laboratory to prevent sharing the results of ALT/AST sensitive clinical data. C3/C4 will also be sent to the central laboratory at Visits 23, 24, 25, 26, 27. For more details please see Section 8.2.12 and Appendix 2. For sites in Japan only: additional local laboratory tests will be collected at Visits 21 and 22, see Appendix 2 for details.

y. On Day 417 (Visit 29.2), only GLDH will be collected.

z. ADA to mini-dystrophin only.

aa. Sites will be responsible for confirming participant eligibility to undergo MRI scanning and gadolinium contrast administration (Section 2.3.3.7). If the site considers gadolinium contrast administration unsafe, or if the participant has a history of allergy to gadolinium, cardiac MRI without contrast administration will be performed. It is important that the investigator discusses with the participant and/or caregivers that a cardiac MRI even under general anesthesia may be required in certain situations (Section 8.2.8). Only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35).

Period	Year 2																			Long-term follow up		Early Discontinuation Visit [e]
Visit Number/Description	Visit 20[a,bb, cc]	Visit 21[bb, cc]	Visit 22[bb, cc]	Visit 23[bb, cc]	Visit 24[bb, cc]	Visit 25[bb,cc] & 26[bb,cc]	Visit 27[bb, cc]	Visit 28[bb, cc]	Visit 29[b, bb, cc]	Visit 29.2[b, bb, cc]	Visit 30[bb, cc]	Visit 30.1[ee, bb,cc]	Visit 30.2[b, bb, cc]	Visit 31[c,cc]	Visit 31.2[b,cc]	Visit 32[b,cc]	Visit 33	Visit 34	Visit 35	Visits 36, 38, 40, 42[d]	Visits 37, 39, 41, 43[d]	
	Year 2, Week 1, Day 1	Year 2, Week 1, Day 2	Year 2, Week 1, Day 4	Year 2, Week 1, Day 6	Year 2, Week 1, Day 7	Year 2, Week 2, Days 8 &9	Year 2, Week 2, Day 10	Year 2, Week 2, Day 14	Year 2, Week 3	Year 2, Week 4	Year 2, Week 5	Year 2, Week 6	Year 2, Week 7	Year 2, Week 9	Year 2, Week 11	Year 2, Week 13	Year 2, Week 18	Year 2, Week 35	Year 2, Week 52	Years 3, 4, 5, 6[d]	Years 3, 4, 5, 6[d]	
Visit Day	390	391	393	395	396	397& 398	399	403	410	417	423	431	437	449	463	479	509	629	749	930, 1290, 1650, 2010[d]	1110, 1470, 1830, 2190[d]	
Visit Window (± days)	3[f]	2[f]	2[f]	2[f]	2[f]	2[f]	2[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	3[f]	7[f]	7[f]	7[f]	30[f]	30[f]	

bb. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not attend Visits 20 to 30.2 and therefore will not perform the corresponding tests and assessments. These participants will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

cc. Cohort 1 participants confirmed to meet exclusion criterion 15 and participants who declined Year 2 IP administration will not receive their protocol-mandated glucocorticoid regimen at Year 2. For details on the retrospective assessment of exclusion criterion 15, please see Appendix 12 and Section 7.2.1.

dd. Following IP administration, participants will remain as inpatients for at least 7 days after the infusion has terminated and will be discharged on Day 397, or later if deemed necessary by the Investigator (see Section 8.2.10).

ee. This visit is for sites in Germany only and only to test cardiac troponin I. Unless clinical concern and/or participant preference and/or the site's institutional review board's preference warrants in-person visit, this visit may be performed remotely, and would include blood collection at or close to the participant's home coordinated by local phlebotomist, as well as phone communication between site staff and participant/caregiver to discuss any adverse events and/or changes to concomitant medications.

ff. A participant who has a muscle biopsy at the Baseline Visit (Visit 2), and their siblings, will undergo two post-Baseline muscle biopsies. The post Baseline muscle biopsies will be performed on Day 360 (Visit 19) in Year 1 and on Day 1830 (Visit 41) during Long Term Follow-Up. If the post-Baseline muscle biopsy cannot be scheduled on the day of Visit 19 or Visit 41, it may be performed at a later date, as long as it is at least 2 weeks before dosing, for the biopsy at Visit 19 and within 1 month of the day of the visit for the biopsy at Visit 41.

gg. Only for sites in Russia

10.17. Appendix 17: Protocol Amendment History

The Protocol Amendment Summary of Changes Table for the current amendment is located directly before the table of contents (TOC). The protocol amendment summary of changes tables for past amendment(s) can be found below:

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
Amendment 14	**07 June 2023**	CCI [redacted] In Section 8.2.7, added instructions that for events of elevated troponin or myocarditis with or without abnormal findings in the initial cardiac MRI, a follow-up cardiac MRI will be performed approximately 3 months after the start of the event. This update was done to ensure adequate follow-up of events of elevated troponin or myocarditis. In Section 8.2.7, added clarification for cases of elevated troponin meeting protocol criteria for further follow-up to repeat troponin and NT-ProBNP tests (or BNP, if NT-ProBNP is not available) approximately every 48-72 hours) until each test returns to Baseline values or reaches a level considered not clinically significant by the investigator. This update was done to ensure adequate follow-up of cases elevated troponin. In Section 8.2.7 and 8.2.8 (for cardiac MRI) clarified that when cardiac images (ECG, echocardiogram, cardiac MRI) are performed during the evaluation of cases of elevated cTn-I meeting protocol criteria for further follow-up, the submission to the central reader should be done in less than 72 hours. This update was done to ensure adequate follow-up of cases elevated troponin.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 6.1 and in Appendix 10, clarified that IV methylprednisolone, oral prednisone, or prednisolone, deflazacort, eculizumab, antiemetics e.g., ondansetron and MenACWY vaccine are not subject to safety reporting in accordance with Japanese regulation requirements. This update was done to align with Japan reporting regulations for non-IP study interventions. In Section 8.1.3, incorporated updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 03 November 2022 to indicate that not only a surgeon but also a healthcare professional with adequate experience, as evaluated by the Sponsor beforehand can perform muscle biopsies in the study. This update was done to address the fact that in some specialized DMD centers muscle biopsies from patients with DMD are performed routinely by neurologists and not by surgeons. In Section 8.2.10, added recommendation to keep the IV line in place for at least 48 hours post IP administration in case IV hydration or treatment is necessary due to nausea, vomiting, anorexia, etc. This recommendation was added to minimize the risk of participants experiencing volume depletion.
Amendment 13	**06 April 2023**	In Section 6.1, updated dosing so that nominal drug concentration is used for dose calculation instead of exact lot specific concentration. This will be implemented only for Year 2 IP administration when instructed by the Sponsor. This change was done to comply with a request by FDA to gain experience with dosing using a nominal titer during the Phase 3 clinical study. In Section 8.2.11, added language to remind investigators to carefully monitor participants with mutations between exons 30-41 or at exon 55 to comply with a request by the French regulatory

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		authority, ANSM, and to align with the language in the ICD and in the IB. In Sections 1.3.1, 1.3.2, 10.9.1.1, 10.9.1.2, 10.10.1.1, 10.10.1.2, 10.14.1, and 10.14.2, added test for anti mini-dystrophin ADA at Visit 12 (Day 21) and Visit 12.2 (Day 28) in Year 1 and at Visit 29 (Day 410) and Visit 29.2 (Day 417) in Year 2 to facilitate the early detection of participants with high titers who may be at high risk to develop an immune reaction against the transgene mini-dystrophin protein expressed in skeletal/cardiac muscle. This would allow an early intervention before overt signs and symptoms have developed. In Sections 10.9.1.1 and 10.9.1.2, updated approximate blood volume at Visit 12 (Day 21) and Visit 29 (Day 410) from 10 ml to 12 ml; and at Visit 12.2 (Day 28) and Visit 29.2 (Day 417) from 2.5 ml to 4.5 ml. The blood volumes collected at these visits have been increased due to the addition of anti mini-dystrophin ADA tests. In Sections 5.3.1 and 5.3.2, added that for participants randomized with delayed IP administration who are re-confirmed to be eligible for Year 1 or Year 2 IP administration, the dose of IP will be re-calculated if there is a change in body weight > ±5% of the prior body weight In Section 6.1, added IMP/NIMP/AxMPs information to existing study intervention table and added specific “Study Intervention(s)” table In Sections 1.3.1, 1.3.2, 8.2.12, Appendix 2 and Appendix 15, incorporated changes to reflect Russian PACL on local and central laboratory testing (19 Dec 2022). Added local labs to Appendix 2. Added Appendix 15 – Russia Appendix

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Sections 1.3.1, 1.3.1, Appendix 2 and Appendix 14, clarified that at Day 42 (Visit 13.1) and at Day 431 (Visit 30.1) only Cardiac Troponin I is assessed. Changed all instances of "ELISpot to dystrophin "to "ELISpot to mini-dystrophin" throughout the document. In Section 3.1, deleted measurement of WPAI caregiver response at Year 1. In Section 10.2, changed "Total neutrophils" to "Absolute neutrophils" in Table 3 – Local Laboratory. In Section 10.4, added "and barrier" to the title. In Sections 10.9.1.1 and 10.9.1.2, corrected the shading to match the other SoA table. In Section 10.9.1.2, corrected the Italy SoA to add Local/Central Lab Testing to Visit 20 In Sections 1.3.1, 1.3.2, 10.9.1.1, 10.9.1.2, 10.10.1.1, 10.10.1.2, 10.14.1, and 10.14.2, footnote "a, clarified that the allowance to repeat screening blood tests with results considered by the Investigator to be transient and inconsistent with the participant's clinical condition refers to blood tests. On the title page, Sections 10.1.1; 10.1.3; 10.1.4; 10.1.5; 10.1.6; 10.1.8, 10.1.9 and 10.1.10, updated to match the current Pfizer protocol template. In Section 5.6, moved text regarding screen failures previously in Section 10.1.3. In Section 1.1, removed all cross-references. In Section 6.1.1, deleted an instance of 'the" repeated in a paragraph.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Throughout the document, all instances of "PF-06939926" were changed to "fordadistrogene movaparvovec" and all instances of "mini dystrophin" were changed to "mini-dystrophin".
Amendment 12	**12 September 2022**	In Section 1.3.1, 1.3.2, 4.1, 4.2.4, 2.3.3.2, 8.1.3, SoA, included an additional muscle biopsy at Day 1830 (Visit 41) for participants with a Baseline muscle biopsy to obtain longer term information on durability of muscle expression and distribution of mini-dystrophin In Section 3.1, added long-term mini-dystrophin expression and distribution endpoints to assess longer term information on durability of muscle expression and distribution of mini-dystrophin In Section 4.2.4, 2.3.3.2, 4, 5.4, 8.1.3, 1.3.1, and SoA, Updated the number of biopsies to be collected to approximately 15, with a potential to collect a maximum of 33 if needed. Due to operational reasons, collection of muscle biopsies in approximately 33 participants is not feasible In Section 4.1, 1.1, and 6.3.1, updated the age caps to indicate that no more than approximately 55% of dosed participants will be included in either of Screening age strata. Additionally, 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. This change was made to achieve a more balanced age distribution in the study so that both age strata are equally represented. In Section 4.2.4, and 9.5, modified the first interim analysis that was to be based on mini-dystrophin expression levels as a surrogate endpoint to instead occur when approximately 30 participants in the FAS complete visits through Week 52 and be based on change from Baseline at Week 52 in the NSAA total score. Due to operational reasons, an interim

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		analysis based on mini-dystrophin expression levels in the first 33 participants is not feasible. These updates enable the potential for an earlier regulatory submission based on the primary endpoint, NSAA. In Section 5.1, Appendix 10.14 and Appendix 12, Updated exclusion criterion # 15 to also exclude patients with a deletion affecting any exon between 56 and 71, inclusive. Following an SAE of myositis reported in this study it was agreed with the E-DMC to exclude participants with deletions affecting any exon between 56 and 71, inclusive, to prevent patients who would be CRIM negative from receiving gene therapy, given that they may be at an increased risk of immune reactions against the mini-dystrophin transgene protein expressed in skeletal and cardiac muscle. In Sections 9.1, 9.2, 9.5, and 1.1, Revised the approach for controlling Type 1 error to include the potential for 2 interim analyses and clarified that a gamma family alpha-spending function with gamma parameter -1 will be used. Added a futility assessment at each interim analysis with gamma (-4) spending function. This was done to ensure that Type 1 error will be controlled across multiple looks at the data and to enable early stopping of dosing additional participants for futility In Appendix 2, and Section 6.5.1, indicated that haptoglobin will also be measured at Visit 19 to provide a pre-dose value of haptoglobin that would help assess changes in haptoglobin that may indicate the development on TMA post Year 2 IP administration. New Appendix 12.2, to provide instructions to sites for the management of participants retrospectively found to meet the updated exclusion criterion # 15, depending on their stage of enrolment and their treatment cohorts.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
Amendment 11	**09 September 2022**	Added Appendix 14: Germany Specific Country Amendment In Section 10.14.3 added inclusion and exclusion criteria from Section 5.1 and 5.2 and added a new inclusion criterion (number 9) only for sites in Germany: "At the Screening Visit (Visit 1), the investigator will discuss and agree with the participant or their legally acceptable representative the potential need for an autopsy, if the participant dies between Year 1 IP administration and during the following 10 years". Rationale: this inclusion criterion has been added to fulfill a request by the German Central Ethics Committee. Added SoA from Section 1.3 to Section 10.14.3 with additional cardiac troponin I at Week 6 for Year 1 and Year 2. Rationale: these visits and assessments had been added to the Germany-specific protocol amendment 9 to fulfill a request by the German Federal Institute for Vaccines and Biomedicines.
Amendment 10	**10 June 2022**	**Country-specific changes as requested by the Japan PMDA.** In Appendix 10, Sections 10.10.1.1 and 10.10.1.2, included a new row to display the visits when cardiac troponin must be assessed by the local laboratory. Rationale: this change has been made as per the request by the Japan PMDA.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Other updates In Appendix 2, clarified that for sites in Japan GLDH must also be analyzed by the central laboratory on Days 2 and 4 (Visits 4 and 5) in Year 1, and on Days 391 and 393 (Visit 21 and 22) in Year 2 even though some of the blood tests on these visits are analyzed by the local laboratory. Rationale: correction of an unintentional omission in protocol amendment 8. In Appendix 2 and in Appendix 10, Section 10.10.1.1, footnote "w" and in Section 10.10.1.2, footnote "s" clarified that haptoglobin, as part of the "Post IP Intensified Safety Monitoring (at Year 1 and Year 2)" is analyzed by the 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. Rationale: additional statement for increased clarity.
Amendment 9	**13 May 2022**	**Country-specific changes as requested by the German Federal Institute for Vaccines and Biomedicines.** • In Sections 1.3.1 and 1.3.2 added new visits: Visit 13.1, Week 6 at Year 1 and Visit 30.1, Week 6 at Year 2 to perform an assessment of cardiac troponin-I. Also added footnote to indicate that the visit may be performed remotely. • Rationale: This change has been made as per the request by the German Federal Institute for Vaccines and Biomedicines.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 05 May 2022. • Sections 1.3.1 and 10.9.1.1, footnotes "e" and "f", and Sections 1.3.2 and 10.9.1.2, footnote "b": removal of instructions for the site to communicate with participants via email when the study visits are performed remotely. Rationale: It has been determined that email communication cannot be used to conduct visits since this is not an appropriate method of data collection, and should not be used to generate source documentation.
Amendment 8	**04 March 2022**	**Incorporation of country-specific changes initially implemented in Germany only via Amendment 7, dated 04 March 2022:** • In Sections 1.3.1, footnote "d", 1.3.2, footnote "a", and 8.2.10, added requirement that participants will be followed up as inpatients for at least 7 days post IP administration. Once enrollment is complete and the last participant has completed 14 days post-Year 1 IP administration, the E-DMC will review the safety information accrued to determine if any changes to the Year 2 IP administration schedule, including need for and length of hospitalization, are required. Additionally, in Sections 1.3.1, footnotes "d," "i," and "j", 1.3.2, footnotes "a," "h," and "i," and 8.2.4, added O2 saturation and specified vital signs will be measured 3 times per day during the inpatient stay post IP administration. Rationale: To optimize follow-up during the initial days post-IP administration so that any AE is promptly identified and managed. This would also allow IV hydration and

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		treatment if there is nausea and/or vomiting that may prevent oral intake of protocol-mandated glucocorticoid regimen, that would decrease the immunosuppression that the participant receives and potentially increase the risk of immune-mediated AEs. In Section 8.2.10, updated the list of laboratory criteria that would require a participant to return to the site within 24 hours to include signs of low perfusion volume. Rationale: To optimize the management of participants who may present with signs related to a cardiac event by allowing early evaluation and management, as needed. In Sections 1.3.1, 1.3.2, and 8.2.12, added local laboratory testing to Baseline (Visit 2), Day 2 (Visit 4), Day 4 (Visit 5), Days 6, Day 8, and Day 10 (Visits 6, 8, and 10) in Year 1, and Day 390 (Visit 20) pre-IP administration, Day 391 (Visit 21), Day 393 (Visit 22), Day 395 (Visit 23), Day 397 (Visit 25), and Day 399 (Visit 27) in Year 2 to assess local cardiac troponin I, or cardiac troponin T when cardiac troponin I is not available. Also added clarification to Section 8.2.12. Local and Central Laboratory Testing and Section 10.2, Appendix 2: Clinical Laboratory Tests, Table 3. Protocol Required Safety Laboratory Assessments. Rationale: Given that local laboratory results are available within a few hours after the blood extraction, while central laboratory results can take up to 4 days to be available, this update will optimize the assessment of potential cardiac injury by allowing a rapid diagnosis and treatment, if required.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Sections. 1.3.1, 1.3.2, 8.2.12, and Appendix 2, added local serum creatinine testing to Baseline Visit (Visit 2), Day 2 and Day 4 (Visits 4 and 5) in Year 1, and Days 390 to 393 (Visits 20 to 22 in Year 2) (local and central laboratory testing). To provide baseline values in case of discrepancy between local and central laboratory results. In Section 5.2, removed the general cardiac criteria from exclusion criterion 9 and added new cardiac exclusion criteria 16 and 17. Rationale: An evaluation by a pediatric cardiologist is required to ensure that participants with clinically relevant cardiac pathologies that may increase the risk of cardiac complications post receipt of gene therapy are not included in the study. To ensure that participants who would not be candidates for mechanical cardiac or respiratory support, or any other invasive intervention for diagnosis or management of a cardiac SAE, are not included in the study, as they would be considered too fragile to be suitable for these potentially required measures. In Section 5.2, updated exclusion criterion 14 to exclude participants with a LVEF <50%, instead of <40%, and to clarify that the screening echocardiogram will be evaluated by the central reader rather than the site for the purpose of determining the LVEF to confirm eligibility. Rationale: To exclude from the study participants who may be at an increased risk of cardiac complications, and to ensure accuracy and consistency in the assessment of LVEF.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 6.1.1, added ineligibility criterion for diagnosis of myocarditis. Rationale: To ensure that participants with a diagnosis of myocarditis that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, are confirmed to be ineligible for IP administration. In Section 7.1, added ineligibility criterion for LVEF <50% on echocardiogram performed at Day 360 (Visit 19), or at the unplanned visit to re-assess eligibility for Year 2 IP administration, as evaluated by the central reader. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants in Cohort 2 who experience a clinically relevant decrease in LVEF that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, do not receive IP (fordadistrogene movaparvovec) in Year 2. In Section 7.1, added ineligibility criterion for diagnosis of myocarditis. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants in Cohort 2 with a diagnosis of myocarditis that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, do not receive IP (fordadistrogene movaparvovec) in Year 2. In Section 7.1, added ineligibility criterion for a participant who is not a candidate for mechanical cardiac or respiratory support, or any other invasive intervention, if indicated for

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		management of an acute event as determined by the cardiologist in consultation with the investigator. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants who are not candidates for invasive measures that may be required for the treatment of some SAEs, for example cardiac SAEs, do not receive IP (fordadistrogene movaparvovec) in Year 2 as they would be considered too fragile to be suitable for these potentially required measures. In Section 8.2.7. Figure 3. Management of Elevated Cardiac Troponin I (cTn-I), added new instructions for the management of participants with elevated levels of cardiac troponin I or T, including requirement for echocardiographic assessments, assessment of NT-ProBNP/BNP, and instructions on when to admit participants with elevated cardiac troponin to the hospital, even if asymptomatic. Updated the time to repeat an elevated cTn-I/ cTn-T from "72-96 hours" to "approximately 48 to 96 hours". Rationale: To improve the ability of the sites and the study team to promptly ascertain if an elevated cardiac troponin reflects an acute cardiac event or if it is related to the fluctuations usually seen in patients with DMD, to allow for prompt management if necessary. In Section 8.2.10, added a reminder for the investigators to discuss with participants and caregivers the potential need for participants with immune-mediated events to be admitted to the intensive care or coronary unit, and to require invasive measures such as the placement of a central catheter, performance of an

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		endomyocardial biopsy, and use of mechanic respiratory or circulatory support. Rationale: To make participants and caregivers aware of the management strategies that may be required in cases of immune-mediated complications, including cardiac events. In Section 1.3.1, removed footnote "e", and in Section 1.3.2, removed footnote "b" due to addition of inpatient hospital stay for at least 7 days post IP administration. **Other changes:** In Sections 1.3.1, footnotes "b" and "f", 1.3.2, footnotes "bb" and "cc", 5.2, 6.5.1, 6.5.2, 7.1, and 8.2.10, provided instructions for the management of Cohort 1 and Cohort 2 participants retrospectively confirmed to meet exclusion criterion 15 after the enrollment and dosing pause implemented on 04 August 2021. Rationale: To ensure that participants in Cohort 1 who had already received fordadistrogene movaparvovec and were retrospectively found to meet exclusion criterion 15 remain in the study for safety monitoring, but do not receive placebo in Year 2, given that it also requires a regimen of high doses of steroids for 3 months and very frequent visits to the site with associated laboratory tests. Rationale: To also ensure that participants in Cohort 2 who received placebo in Year 1 and would receive fordadistrogene movaparvovec in Year 2 are withdrawn from the study to allow them to pursue other treatment(s).

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 1.3.2, increased the visit window for Day 390 (Visit 20) from ± 2 days to ± 3 days. Rationale: To give sites additional flexibility for Year 2 IP administration. In Section 5.3.2, added instructions on how to manage participants with delayed Year 2 IP administration after the enrollment and dosing pause implemented on 21 December 2021 is lifted. Rationale: To be able to re-evaluate Year 2 IP administration eligibility. In Section 8.1.3, added statement to consider performing a muscle biopsy to aid diagnosis and/or management in the event of an SAE affecting skeletal and/or cardiac muscle, to comply with a commitment made to the French regulators, National Agency for the Safety of Medicines and Health Products. This update is now applied globally. Rationale: To be able, when possible, to obtain relevant information for the diagnosis and management of these SAEs. In Section 5.2, relocated specific criteria for retrospective assessment of exclusion criterion 15 to a newly added Appendix 12. In Sections 1.3.1, footnote “hh”, and 1.3.2, footnote “aa”, added clarification to specify only participants with a pre-IP administration cardiac MRI will have a follow-up cardiac MRI on Day 360 (Visit 19) and on Day 749 (Visit 35). In Section 6.3.3, removed exclusion criterion 15 as it is not sensitive clinical data.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 8.1.8, clarified that after certification, a Rater ID will be provided to each CE. The CE is responsible for recording their Rater ID on each completed worksheet. In Section 9.1.1, corrected estimand definitions by removing "in all randomized participants". Rationale: To align with the previously revised definition of the FAS. In Section 10.9.1, incorporated all changes consistent with Sections 1.3.1 and 1.3.2. Provided clarifying text and corrected typographical and grammatical errors where necessary. Rearranged rows in SoA and reformatted Table 3 in Appendix 2 for more clarity. In Section 5.3.1, modified to specify a second unplanned visit will only be needed for participants with a positive NAb to AAV9 test at the Screening Visits (Visit 1). **Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 24 January 2022:** Modified Section 5.3 heading to "Management of Participants Post Enrollment and Dosing Pause" and added new subheadings 5.3.1. Study and Year 1 IP Administration Eligibility and 5.3.2. Year 2 IP Administration Eligibility. In Sections 1.3.2, footnotes "a" and "q", 5.3.2, and 6.5.1, provided instructions on how to manage participants with delayed Year 2 IP administration during the screening, randomization, and dosing pause, implemented on 21 December 2021.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 8.2.7, clarified that given that the central laboratory is using a new cardiac troponin assay (Beckman) with a different upper limit of normal (ULN) than that previously used (Centaur), the instructions for further assessments of participants with an absolute level of cardiac troponin of 1.5 ng/ml are now presented as the difference between the present value of cardiac troponin and the ULN, and not an absolute value. The current criterion is equivalent to the previous one, given that the absolute number of 1.5 ng/ml is 50X > the ULN of the previous assay. **Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 13 January 2022:** In Section 1.3.1 Schedule of Activities Footnote "f" Visit 18, Section 4.1 Table 1, Section 6.1.1 Administration, and Section 6.2.1. Preparation and Dispensing, added text to prevent the dose of IP being calculated and IP being shipped to the site during a study dosing pause, weight will not be entered in the interactive response technology drug management system during the study dosing pause. Once the study is re-started, sites will be able to enter an updated weight in the interactive response technology drug management system to allow the calculation of the dose of IP and trigger the shipment of IP to the site. **Incorporation of updates made by the Belgium Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 07 December 2021. These updates are now applied globally:** CCI [redacted]

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		CCI [redacted] **Incorporation of a requirement by MHRA and communicated to sites in UK via a Dear Investigator Letter dated 07 December 2021. These updates are now applied globally:** • In Section 9.5.1 Data Monitoring Committee, clarified that if the trial is temporarily paused, halt notification will be submitted to the regulatory authorities within the regulatory timelines set in the current applicable regulations, and the trial restart will be only possible after regulatory approval via a substantial amendment if needed. **Incorporation of updates made by the Japan Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 02 November 2021:** Removed Section 10.10.2. Viral Vector Shedding Analysis and reference to Section 10.10.2 within Section 8.8.5 since it was considered that the shedding profile of fordadistrogene movaparvovec was clarified in the ongoing Phase 1b study, the viral shedding analysis for all Japanese participants in accordance with the Cartagena Act Type I use regulations is not required, and the provisions of the study protocol will be applied to Japanese participants.
Amendment 7	**04 March 2022**	**Country-specific changes implemented in Germany only:** • In Sections 1.3.1, footnote "d", 1.3.2, footnote "a", and 8.2.10, added requirement that participants will be followed up as inpatients for at least 7 days post IP administration. Once enrollment is complete and the last participant has completed 14 days post-Year 1 IP

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		administration, the E-DMC will review the safety information accrued to determine if any changes to the Year 2 IP administration schedule, including need for and length of hospitalization, are required. Additionally, in Sections 1.3.1, footnotes "d," "i," and "j", 1.3.2, footnotes "a," "h," and "i," and 8.2.4, added O2 saturation and specified vital signs will be measured 3 times per day during the inpatient stay post IP administration. Rationale: To optimize follow-up during the initial days post-IP administration so that any AE is promptly identified and managed. This would also allow IV hydration and treatment if there is nausea and/or vomiting that may prevent oral intake of protocol-mandated glucocorticoid regimen, that would decrease the immunosuppression that the participant receives and potentially increase the risk of immune-mediated AEs. In Section 8.2.10, updated the list of laboratory criteria that would require a participant to return to the site within 24 hours to include signs of low perfusion volume. Rationale: To optimize the management of participants who may present with signs related to a cardiac event by allowing early evaluation and management, as needed. In Sections 1.3.1, 1.3.2, and 8.2.12, added local laboratory testing to Baseline (Visit 2), Day 2 (Visit 4), Day 4 (Visit 5), Day 6, Day 8, and Day 10 (Visits 6, 8, and 10) in Year 1, and Day 390 (Visit 20) pre-IP administration, Day 391 (Visit 21), Day 393 (Visit 22), Day 395 (Visit 23), Day 397 (Visit 25), and Day 399 (Visit 27) in Year 2 to assess local cardiac troponin I, or cardiac troponin T when cardiac troponin I is not available. Also added

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		clarification to Section 8.2.12. Local and Central Laboratory Testing and Section 10.2, Appendix 2: Clinical Laboratory Tests, Table 3. Protocol Required Safety Laboratory Assessments. Rationale: Given that local laboratory results are available within a few hours after the blood extraction, while central laboratory results can take up to 4 days to be available, this update will optimize the assessment of potential cardiac injury by allowing a rapid diagnosis and treatment, if required. In Sections. 1.3.1, 1.3.2, 8.2.12, and Appendix 2, added local serum creatinine testing to Baseline Visit (Visit 2), Day 2 and Day 4 (Visits 4 and 5) in Year 1, and Days 390 to 393 (Visits 20 to 22 in Year 2) (local and central laboratory testing). To provide baseline values in case of discrepancy between local and central laboratory results. In Section 5.2, removed the general cardiac criteria from exclusion criterion 9 and added new cardiac exclusion criteria 16 and 17. Rationale: An evaluation by a pediatric cardiologist is required to ensure that participants with clinically relevant cardiac pathologies that may increase the risk of cardiac complications post receipt of gene therapy are not included in the study. To ensure that participants who would not be candidates for mechanical cardiac or respiratory support, or any other invasive intervention for diagnosis or management of a cardiac SAE, are not included in the study, as they would be considered too fragile to be

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		suitable for these potentially required measures. In Section 5.2, updated exclusion criterion 14 to exclude participants with a LVEF <50%, instead of <40%, and to clarify that the screening echocardiogram will be evaluated by the central reader rather than the site for the purpose of determining the LVEF to confirm eligibility. Rationale: To exclude from the study participants who may be at an increased risk of cardiac complications, and to ensure accuracy and consistency in the assessment of LVEF. In Section 6.1.1, added ineligibility criterion for diagnosis of myocarditis. Rationale: To ensure that participants with a diagnosis of myocarditis that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, are confirmed to be ineligible for IP administration. In Section 7.1, added ineligibility criterion for LVEF <50% on echocardiogram performed at Day 360 (Visit 19), or at the unplanned visit to re-assess eligibility for Year 2 IP administration, as evaluated by the central reader. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants in Cohort 2 who experience a clinically relevant decrease in LVEF that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, do not receive IP (fordadistrogene movaparvovec) in Year 2.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 7.1, added ineligibility criterion for diagnosis of myocarditis. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants in Cohort 2 with a diagnosis of myocarditis that could increase the risk of cardiac complications after treatment with fordadistrogene movaparvovec, do not receive IP (fordadistrogene movaparvovec) in Year 2. In Section 7.1, added ineligibility criterion for a participant who is not a candidate for mechanical cardiac or respiratory support, or any other invasive intervention, if indicated for management of an acute event as determined by the cardiologist in consultation with the investigator. This applies only for participants in Cohort 2, confirmed by the unblinded medical monitor. Rationale: To ensure that participants who are not candidates for invasive measures that may be required for the treatment of some SAEs, for example cardiac SAEs, do not receive IP (fordadistrogene movaparvovec) in Year 2 as they would be considered too fragile to be suitable for these potentially required measures. In Section 8.2.7. Figure 3. Management of Elevated Cardiac Troponin I (cTn-I), added new instructions for the management of participants with elevated levels of cardiac troponin I or T, including requirement for echocardiographic assessments, assessment of NT-ProBNP/BNP, and instructions on when to admit participants with elevated cardiac troponin to the hospital, even if asymptomatic. Updated the time to

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		repeat an elevated cTn-I/cTn-T from "72-96 hours" to "approximately 48 to 96 hours". Rationale: To improve the ability of the sites and the study team to promptly ascertain if an elevated cardiac troponin reflects an acute cardiac event or if it is related to the fluctuations usually seen in patients with DMD, to allow for prompt management if necessary. In Section 8.2.10, added a reminder for the investigators to discuss with participants and caregivers the potential need for participants with immune-mediated events to be admitted to the intensive care or coronary unit, and to require invasive measures such as the placement of a central catheter, performance of an endomyocardial biopsy, and use of mechanical respiratory or circulatory support. Rationale: To make participants and caregivers aware of the management strategies that may be required in cases of immune-mediated complications, including cardiac events. In Section 1.3.1, removed footnote "e", and in Section 1.3.2, removed footnote "b" due to addition of inpatient hospital stay for at least 7 days post IP administration.
Amendment 6	**01 September 2021**	In Sections 1.1, 4.1, 5.4, and 9.2, clarified that the study size is now approximately 99 participants in the FAS. To ensure that the study has adequate power for the primary endpoint analysis. In Sections 1.3.1, 1.3.2, 6.3.3, and 10.9.1, added a new ADA to mini-dystrophin assessment at Day 14 in Year 1 and Year 2; and clarification that ADA to

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		mini-dystrophin will be reviewed by the unblinded medical monitor on an ongoing basis. As recommended by the E-DMC to optimize safety monitoring. In Sections 1.3.1, 1.3.2, and 10.9.1, added cardiac troponin I assessments to Days 28, 48, 74, and 90 in Year 1 and Days 417, 437, 463, and 479 in Year 2 in the Schedule of Activities. Removed cardiac troponin I assessments on Day 7 in Years 1 and 2 in the Schedule of Activities due to addition of central laboratory assessments on these days in Section 10.2 (Appendix 2). To optimize the monitoring for myocardial injury during the period when the risk of cellular immune response is anticipated to be most likely. In Sections 1.3.1, 1.3.2, 3.2, and 10.9.1, added cardiac MRI assessments to Screening Visit (Visit 1) or Baseline (Visit 2) and Week 52 in Years 1 and 2, relevant footnotes to Schedule of Activities, and associated objectives and endpoints. To establish presence or absence of cardiac injury prior to delivery of gene therapy, and to aid in interpretation of cardiac MRI that may be performed in response to adverse events. In Sections 1.3.1, 1.3.2, 5.3, 5.6, 7.1, and 10.9.1, clarified that participants who exceed the time between the Screening Visit (Visit 1) and the Day 1 Visit (Visit 3), or the time between Day 360 Visit (Visit 19) and the planned Day 390 Visit (Visit 20) due to operational or administrative reasons (eg, enrollment pause due to regulatory or safety review, operational issues causing significant delays) will not be screen failed/withdrawn from the study, but will repeat some tests and assessments to

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		re-confirm study eligibility/IP administration eligibility criteria, and to rule out significant changes in key tests and assessments. At the time of the implementation of the enrollment/dosing pause, there were 3 participants who had started the screening process, but had not yet been randomized, and 12 participants who had been randomized, but had not yet received IP. To avoid withdrawing participants who may still be eligible for study entry, they may be re-assessed for study entry at unplanned visits. If they still meet study entry criteria, they will continue participating; if, following the re-assessment, they do not meet study entry criteria, they will be screen failed/withdrawn. In Sections 1.3.1, 1.3.2, and 10.9.1, added additional measurements of CK at Days 21, 28, 48, and 74 at Year 1, and at Days 410, 417, 437, and 463 at Year 2. To optimize the monitoring, by the unblinded medical monitor, of markers of muscle injury, during the period when the risk of cellular immune response is anticipated to be most likely. In Sections 1.3.1 (footnote bb.), 5.3 (new), 7.1, and 10.9.1, clarified that IP administration can only take place if there is a NAb to AAV9 test from a sample collected 55 days or less before the dosing date. Given the enrollment/dosing pause, the NAbs to AAV9 will be repeated more than once to ensure that the last collection has been taken no more than 55 days before dosing. In Section 2.3.2, updated to indicate that cases of skeletal muscle and cardiac injury have been

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		observed in clinical studies of fordadistrogene movaparvovec. To inform investigators that the events previously described as potential risks have now been reported, to increase awareness of the need to carefully monitor for these events. Added a new Section 2.3.3.7 Gadolinium to describe the risks related to use of gadolinium for the cardiac MRI. In Section 5.2, added clarity to Exclusion Criterion 9 that a cardiology consultation should be obtained to evaluate any findings on cardiac history or imaging to help determine eligibility for the study. To ensure that a participant with a cardiac finding during the screening period is evaluated by a pediatric cardiologist, and that the risk:benefit ratio of enrolling such a participant is carefully considered in this circumstance. In Section 5.2, added new exclusion criterion #14 for LVEF <40%. Added clarification to Section 8.2.6 to specify LVEF below 50% at any visit after screening. To exclude participants with high cardiac risk. In Section 5.2, added exclusion criterion 15 for participants with specific mutations in the dystrophin gene considered to increase the risk of immune-mediated adverse reactions. Recommendation by the E-DMC based on the review of the immune and genetic data from studies C3391001 and C3391003.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Sections 5.2, 6.3.3, and 7.2, added instructions for the retrospective assessment of exclusion criterion 15. This key entry criterion must be evaluated for all study participants, to help minimize the risk of immune-mediated adverse reactions. In Section 5.2, added "investigational vaccine" to "investigational drug" in exclusion criterion 3. This change was also applied in Section 6.1.1 #3. For completion of the exclusion criterion. Added new Section 5.3 ("Siblings" moved to Section 5.4), added list of tests and assessments to be repeated in participants who exceed the 90-day period between screening and dosing in Year 1, or the period between Visit 19 and Visit 20 in Year 2. Some tests and assessments may have clinically significant variations in 90 days, that could make a participant previously eligible for study/IP administration no longer eligible; and/or affect the interpretation of the study. In Section 8.2.7, amended instructions for actions based on tests/evaluations for an elevated cardiac troponin I in the troponin algorithm in Figure 3 Management of Elevated Cardiac Troponin I (cTn-I) values to specify the conditions in which a cardiac MRI will be performed. For cTn-I levels and changes that are atypical for DMD, a cardiac MRI would be useful in determining the nature of the cardiac involvement and whether medical intervention is warranted. Added a new Section 8.2.8 Cardiac MRI to include instructions on collection of cardiac MRIs.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		In Section 8.2.10, clarified that the redacted medical records with the results of the local laboratory tests that the sites send to the sponsor must be password protected. To protect the privacy of the study participants. Added a new Section 8.2.11. Additional Safety Monitoring to include monitoring of signs and symptoms of cardiac injury. To optimize the monitoring for cases of muscle weakness and/or myocarditis to help early detection and management if needed. In Sections 1.3.1, 1.3.2, 3.1, 8.9, and 10.9.1, added Healthcare Resource Utilization Questionnaire – Caregiver (HRU:CG) and Work Productivity and Activity Impairment DMD Questionnaire – Caregiver (WPAI:DMD Caregiver), and associated objectives and endpoints. To assess the indirect effects that treatment with fordadistrogene movaparvovec may have on caregivers. In Sections 1.3.1, 1.3.2, 8.1.7.1.4, and 10.9.1, added EQ-5D-5L questionnaire. To assess the indirect effects that treatment with fordadistrogene movaparvovec may have on quality of life for caregivers. In Section 8.3.5.1, specified that pregnancy in a female household member of a study participant must be reported if the exposure through viral shedding occurred within 2 months after the participant's dosing, and a month prior to or during pregnancy.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		This is a program level decision based on the available data on viral vector shedding from the Phase 1 study. In Section 9.3, revised the definition of the FAS to additionally require that participants be dosed with IP on Day 1 (Year 1 Day 1) and to specify that participants who meet exclusion criterion 15 will be excluded. Clarified that participants meeting exclusion criterion 15 will be included in the safety populations. To align the analysis populations with the revised study population following re-evaluation of the participants who were randomized but not dosed, at the time of implementation of the enrollment and dosing pause, and with the addition of exclusion criterion 15. In Section 9.5, added instructions that, in the event of a serious safety issue, the sponsor may determine that screening, randomization, and/or dosing are paused until the E-DMC reviews the relevant data, and makes recommendations for the study conduct. CCI [redacted] In Section 10.9 (Appendix 9), correction of blood volume values due to re-configuration of testing tubes by the central laboratory vendor. It does not increase the approximate total volume calculated per participant, which was updated in Section 8. Added new Section 10.12 (Appendix 12) to include a description of the general outline of a post-approval, long term follow up study.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Requested by the Italian regulatory authority. Added new Section 10.13 (Appendix 13) Protocol Amendment History to move past amendment history from Protocol Amendment Summary of Changes Table.
Amendment 5	**14 April 2021**	In Section 1.3.1, added new row to Schedule of Activities to inform caregivers about study C3391007 for US sites. Study C3391007 was also added to the Section 8.8.6 heading. In Section 1.3.1, clarified in the Schedule of Activities that, when agreed by the site, testing for NAb to AAV9 could be done on the first day of Screening (Visit 1); and that only participants with a negative test for NAb to AAV9 will complete the rest of Screening (Visit 1). • To reduce the burden of additional tests and assessments for participants who are ineligible for study participation. In Sections 1.3.1 and 1.3.2, added additional visits to assess GLDH and chemistry panel to optimize the monitoring of hepatic safety in line with the product information of Zolgensma. In Section 2.3.3.1, added text to describe the potential risk of adrenal insufficiency during the tapering of glucocorticoids for the protocol-mandated glucocorticoid regimen. Added new Section, 2.3.3.6, to describe the risks related to sorbitol since each intravenous infusion of fordadistrogene movaparvovec (and infusion of placebo) contains 5% sorbitol. In Section 5.2, added a new exclusion criterion for participants with known hypersensitivity to any of the components of the IP or solution for infusion,

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		such as hypersensitivity to albumin or a diagnosis of hereditary fructose intolerance (HFI). • To prevent the enrollment of participants at risk of hypersensitivity reactions. In Section 5.2, added a new exclusion criterion to align with the guidance to consider treatment with eculizumab. In Section 5.2, deleted exclusion criterion #8 and #9. These therapies (vaccines, except live attenuated; interferon; systemic antivirals and immunosuppressors) will be prohibited only for 30 days before Day 1 (Visit 3) and for the first 2 years of the study. This update is also reflected in Sections 6.1.1, 6.5.1, 6.5.2, and 7.1. • To increase flexibility in the administration of vaccines and the above-mentioned medications, while still ensuring adequate time for any effect on the immune system to be stabilized before IP administration. In Section 5.2, updated in exclusion criterion #7 the prohibition for receipt of live attenuated vaccines from 90 to 30 days before Screening Visit (Visit 1) and clarified that these vaccines are prohibited for 90 days before IP administration. This update is also reflected in Sections 6.1.1, 6.5.1, and 7.1. • To increase flexibility in the administration of vaccines while still ensuring adequate time for any effect on the immune system to be stabilized before IP administration. In Section 5.2, updated exclusionary level of cystatin C to >1.2 x ULN. This update is also reflected in Sections 6.3.3 and 7.1. • To account for elevated values as a result of treatment with steroids, that do not reflect

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		renal impairment, at Screening and at the time of evaluation of Year 2 IP administration eligibility. In Section 5.3, clarified that 2 (or more) brothers can receive IP at different times as long as the 2 (or more) brothers are kept strictly separated from each other until all have received IP. This update is also reflected in Section 6.3.1. • To allow flexibility in the dosing schedule, while still minimizing the risk of development of neutralizing antibodies to AAV9 in the sibling who has not yet received IP. Updated Section 5.4.2 to indicate that participants should be monitored to determine if they pass urine at least once during a 12-hour period or if they have a significant change in urine output in less than 24 hours. These updates are also reflected in Section 8.2.9. • To allow early identification of participants with potential kidney injury, and to align with the guidance to consider treatment with eculizumab. In Section 6.1.1, added guidance on how to proceed when participants have hypersensitivity reactions during IP infusion. In Section 6.2.1, clarified that IP should be dispensed once participants have been confirmed to be eligible and admitted to the site and added a recommendation to prepare IP solution as close to the time of dosing as possible. In Section 6.3.3, clarified that the unblinded medically qualified monitor (unblinded medical

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		monitor) will not review the results of ADA and ELISpot for each participant on an ongoing basis. • The results of these tests do not have identified thresholds to initiate clinical actions and are therefore not relevant for safety monitoring. In Section 6.5.1, added an additional step of 1.5 mg/kg/day of prednisone/prednisolone for 14 days to the tapering of glucocorticoids during the protocol-mandated glucocorticoid regimen, to minimize the risk of adrenal insufficiency. The total duration of the protocol-mandated glucocorticoid regimen is now 90 days. This update is also reflected in Sections 1.3.1, 1.3.2, 2.3.2, and 6.1.1. In Section 6.5.1, clarified that IV glucocorticoids can be administered per the clinical judgement of the investigator to participants with vomiting. • To ensure that participants with vomiting and unable to tolerate oral medications receive adequate treatment with glucocorticoids. In Section 6.5.1, updated prohibition time for live attenuated vaccines to no later than 90 days before investigational product (IP) administration. • To align with the updated exclusion criterion #7. In Section 6.5.1, updated prohibition time for meningococcal vaccine from no later than 2 weeks to 30 days before investigational product (IP) administration. • To align the time restrictions with other inactivated vaccines. In Section 6.5.1, added guidance on when to administer an mRNA, or DNA-based, or

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		non-replicating viral vector vaccine (eg, against SARS-CoV-2). This update is also reflected in Section 7.1. • To allow participants to receive a vaccine against SARS-CoV-2 if indicated, while minimizing the potential impact on the safety and efficacy of fordadistrogene movaparvovec. In Section 6.5.2, added new text to indicate that antiviral therapy and interferon can be administered to treat an acute viral infection (eg, COVID-19). In Section 8.2.9, updated platelet criterion for which participants will be required to return to the site for evaluation from <100 x 10^3/µl to <75 x 10^3/µl. • To align this criterion with the guidance provided to consider start of treatment with eculizumab. • In Section 8.2.9, added a description of the process to review local laboratory reports. In Section 8.3.1, added language. • To align with new template requirements. In Sections 8.3.5.1, 8.3.5.2, and 8.3.5.3, updated language for Exposure During Pregnancy and Occupational Exposure, and added language for Exposure During Breastfeeding. • To align with new template requirements. Added Sections 8.3.7 through 8.3.9. • To align with new template requirements. In Section 8.3.10, updated time period for notification of the Sponsor from immediately to

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		within 24 hours in the event of a medication dosing error. • To align with new template requirements. In Section 8.4, updated overdose language. • To align with new template requirements. In Section 8.9, removed language that described a study to assess caregivers' burden as it has been canceled. In Sections 10.3.2 and 10.3.3, updated the Definition of SAE to include suspected transmission via a Pfizer product of an infectious agent, updated the Recording/Reporting and Follow-up of AEs and/or SAEs to specify all AEs/SAEs associated with exposure during pregnancy or breastfeeding be recorded on the CRF, and note all SAEs associated with exposure during pregnancy or breastfeeding and all AEs/SAEs associated with occupational exposure should be reported on the CT SAE Report Form to Pfizer Safety within 24 hours of awareness. • To align with new template requirements. Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 16 March 2021: • In Sections 1.3.1 and 1.3.2, added cardiac troponin I assessments to Visits 7 and 13 in Year 1 and Visits 24 and 30 in Year 2 to Schedule of Activities. • Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 19 March 2021:In Section 6.5.1, modified the wording to allow investigators to change the dose of glucocorticoids at any

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		time, if medically required, and in consultation with the Sponsor. • To allow the investigators to change the doses of glucocorticoids to treat not only an immune reaction, but also other medical issues. Additionally, allowing these changes at any time, instead of only during the first 2 months, would permit treatment of late immune reactions, if needed. Incorporation of updates made by the Japan Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 14 July 2020: • In Sections 6.1 and 10.10.1, added the reporting of Interventional Study Defects applicable to Japanese investigators and Japanese sites per the Japanese regulation: "Act on Securing Quality, Efficacy and Safety of Products including Pharmaceuticals and Medical Devices." Incorporation of updates made by the Japan Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 01 September 2020: • In Sections 8.8.5 and 10.10.2, specified viral vector shedding samples for participants randomized in Japan will be collected from all participants, rather than limiting it to approximately 45 initially treated participants. Incorporation of updates made by the Japan Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 09 November 2020:

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		• In Sections 1.3.1, 1.3.2, and Appendix 2, added new text requested by PMDA to indicate blood and urine samples collected at Visits 4 and 5 in Year 1 and Visits 21 and 22 in Year 2 will be sent to the local and central laboratory for sites in Japan. • In Sections 4.1 and 10.10.3, added new text requested by PMDA to ensure at least 14 days between IP administration for consecutive participants. • In Sections 8.2.9 and 10.10.4, added new text agreed upon by PMDA to indicate participants randomized from sites in Japan will be admitted to hospital for at least 14 days after IP administration and will be discharged if there are no ongoing adverse events that require medical management. • Incorporation of updates made by the Japan Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 14 December 2020: • In Sections 8.3.4 and 10.10.5, added new text requested by PMDA to specify the sponsor will report SAEs that impact study status to the Japan sites within approximately 24 hours of Pfizer Japan receipt of the report. • In Sections 10.1.1.1 and 10.10.6, added new text requested by PMDA to specify information regarding any prohibition or restriction imposed by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the investigational product, should be shared

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		with Japan sites approximately 24 hours after Pfizer Japan is aware of this information. Inclusion of changes made upon regulatory authority request initially implemented via Amendments 2, 3, and 4 (listed below; except for blood volume to be drawn per visit in Section 10.9. Appendix 9. Italy-Specific Country Amendment). Other minor clarifications: In Sections 1.1 (Number of Participants) and 9.2, updated language to better align the sample size estimation with the primary analysis methodology. In Section 2.2.1, updated with text from the recent RMAT. In Section 6.1.1, clarified that the temporary restrictions for receipt of influenza vaccination also apply to other inactivated vaccines (eg, influenza, meningococcus, pneumococcus, Haemophilus influenzae vaccination). In Section 8, added text to provide guidance to investigators on what tests to prioritize at each visit when blood collection cannot be completed. In Section 8.1.1, added new text to indicate the assigned master physiotherapist may request additional visits to be video recorded and reviewed if CE re-training is required for North Star Ambulatory Assessment. In Section 8.1.4, clarified that trained respiratory therapists can also perform the respiratory tests, if allowed by the Sponsor. In Appendix 2, added text to provide guidance to the study sites to minimize the risk of complication due to venipuncture.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Added Appendix 11 for implementation of alternative measures during public emergencies, including the COVID-19 pandemic. Other minor corrections.
Amendment 4	28 December 2020	Country-specific changes as requested by the German Federal Institute for Vaccines and Biomedicines. • Additional information to the text describing the rationale and the analysis plan for the potential interim analyses in Section 9.5. Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 21 December 2020. • In Section 1.3.1 Addition of a footnote "bb" to the NAb to AAV9 test at the Baseline Visit (Visit 2) to indicate that the analysis and review of NAb to AAV9 from the sample drawn at the Baseline Visit (Visit 2) will only be required if the time between the Screening Visit (Visit 1) and Day 1 (Visit 3) is anticipated to be more than 55 days. As a result of a reduction in the time to deliver Investigational Product (IP) to the site, the time between the first test of NAb to AAV9 and the day of IP administration will be less than initially anticipated, up to 90 days, and hence a second NAb to AAV9 at the Baseline Visit (Visit 2) is not required to confirm eligibility for Year 1 IP administration. • Update the footnote "c" in Section 1.3.1, corresponding to the Baseline Visit (Visit 2), to reflect the reduced time for delivery of Investigational Product to the site.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
Amendment 3	24 November 2020	Country-specific changes as requested by the Italian Medicines Agency. • Addition in Appendix 10.9 of a new exclusion criterion (#14), for participants with known hypersensitivity to any of the components of the study drug or solution for infusion. • Addition of information on blood volume to be drawn per visit in Appendix 10.9. Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 01 October 2020: • Clarification in Section 5.2, exclusion criterion #2 that patients receiving benefit from an ongoing treatment designed to increase dystrophin expression should not discontinue it in order to enroll in the study. Additionally, the time during which any treatment designed to increase dystrophin expression is prohibited has been changed from the first 2 years of the study to the first 52 weeks of the study. This change was already incorporated in the UK-specific Amendment 2. • Clarification in exclusion criterion #10, Section 5.2, that one of the hematological abnormalities mentioned consists of a platelet level <150 x10^3/µl. This change also applies to Section 6.3.3 and Section 7.1. This change was already incorporated in the UK-specific Amendment 2. • Clarification, in Section 8.2.9 that sites will not be made aware of the results of C3 and C4 on a routine basis and, in consequence, reduced complement levels will not be a

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		criterion for expedited participant evaluation at the site within 24 hours. Knowledge of the levels of C3 and/or C4 is not considered necessary for clinical decision making. The unblinded medical monitor will not share those results routinely with the sites and the sponsor unless, in their clinical judgement, a significant or unexpected abnormality should be communicated. • Clarification in Section 8.1.3 that biceps brachii muscle biopsies will be collected in approximately the first 33 participants randomized into Cohorts 1 and 2 (and their siblings) from sites that have been trained and certified by the Sponsor/Sponsor designee to collect open muscle biopsies in this study. This update is also reflected in Section 1.3.1, footnote "n" and in Section 2.3.3.2. It was initially anticipated that sites in the United States would be activated first and would randomize the first approximately 33 participants who must have a biceps brachii biopsy collected, as per the protocol. Therefore, training and certification by the Sponsor/Sponsor designee to collect open muscle biopsies was planned in advance for these sites. Due to unforeseen circumstances, the activation of sites in the United States has been delayed and therefore sites in other countries will be trained to collect biceps brachii biopsies. • Addition of details about the flushing of the IV line after IP administration in Section 6.1.1.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Important information for the completion of IP administration. • Correction of an unintentional mistake in Section 6.5.2 that states that systemic antiviral and/or interferon therapy will be prohibited from the time of signing the informed consent until the end of Year 2. The instructions should indicate that after Year 1 Investigational Product administration, the use of systemic antiviral and/or interferon therapy is only prohibited within 30 days prior to Year 2 IP administration, and for the first 2 months after each IP administration. The corrected text in Section 6.5.2 is in alignment with the text in exclusion criterion #8, Section 5.2. • Correction in Section 8.4 of the text about overdose to clarify that for this study, any dose of fordadistrogene movaparvovec greater than a single administration of 2E14 vg/kg will be considered an overdose, even if it occurs outside of a 24 hour time period. • In Section 8.1.4 change the formula to calculate %pFVC from Hankinson et al., 1999 to Qanjer et al., 2012. The updated equation is better suited to North and East Asian populations that will be included in the study.
Amendment 2	05 October 2020	Country-specific changes as requested by the UK Medicines and Healthcare products Regulatory Agency. Clarified in Section 5.2, criterion 2, that stopping a therapy to increase dystrophin expression in a patient who benefits from it, in order to enter the study, is not recommended.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		• To stress that decisions and actions regarding medication choice must be made by each patient and family in consultation with their physician with the best interest of the patient in mind. Clarified in Section 5.2, criterion 10 and in Section 7.1, criterion 2, that a platelet level <150 x10^3/µl is part of the hematological abnormalities mentioned. • Given the observation of reductions in platelet levels following administration of gene therapy in study C3391001, to reduce the risk that a decrease in platelet count reaches levels that pose a risk to the participant. Clarified in Section 5.2 and in Section 6.5.2 that the use of a therapy to increase dystrophin expression will be prohibited only during the first 52 weeks of the study. • To allow a robust primary analysis without confounding factors, while at the same time give participants the opportunity to start a therapy designed to increase dystrophin expression, if considered necessary, after Day 360 (Visit 19). Incorporation of updates made by the Protocol Administrative Changes and Clarifications for Study C3391003 letter, dated 17 June 2020: Removed the requirement to perform the post-baseline muscle biopsy at Day 60 (Visit 14). • Upon review of relevant data from the ongoing Phase 1b study, C3391001, it was determined that 1 year was the best timing for the post-baseline biopsy to be able to

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		demonstrate durability of the effect of gene therapy on mini-dystrophin expression. Removed the allowance to perform a needle biopsy. • Upon discussion with relevant experts, it has been confirmed that performing an open muscle biopsy is a safe and well tolerated procedure and is preferable for ensuring a consistent and high quality sample. Added in Section 6.3.3 a statement to request that clinical evaluators who perform and score the NSAA should not have access to the participant´s medical records and/or to the database. • Knowledge of the occurrence of certain AEs/SAEs and/or laboratory changes could lead to the functional unblinding of the clinical evaluators and it could bias the scoring of the functional assessments that they perform. Added in Section 6.3.3- Select safety and immunogenicity results- a sentence to the paragraph relating to a situation when a participant in Cohort 2 presents with a positive test for NAb to AAV9 at Day 34 (Visit 13): “If this situation occurs while the study is still accruing participants, an additional 2 participants may be randomized for each Cohort 2 participant who is withdrawn.” • It is expected that it will be extremely rare for a participant in Cohort 2 to test positive for NAb to AAV9 at Day 34; however, to account for the potential for missing data specifically for Cohort 2 participants, beyond the 10% dropout already assumed for the

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		study, additional participants may be randomized. Section 8.1.6: Changed one part of the definition of loss of ambulation after Screening (Visit 1), to be evaluated by the walk item in the NSAA rather than by the 10 meter run/walk item. • The incorrect NSAA item to determine loss of ambulation had been selected given that a score of 0 in the 10 meter run item can be given to a child who is still able to walk. Removed the following language in Section 8.2.8: "If laboratory values from non-protocol specified laboratory assessments performed at the institution's local laboratory require a change in participant management or are considered clinically significant by the Investigator (eg, SAE or AE), then the results must be recorded in the CRF". • To align the protocol with the CRF and the CRF completion guidelines. Replaced the following language in Section 8.3.1.2: "Medical occurrences that begin before the start of study intervention but after obtaining informed consent will be recorded on the Medical History/Current Medical Conditions section of the case report form (CRF), not the AE section" by the updated language: "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, will be recorded on the AE section of the CRF". • To align the protocol with the CRF and the CRF completion guidelines.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Corrected typographical mistakes and added clarifying text when needed.
Amendment 1	18 March 2020	Added physical examination to Day 2 Visit in Year 1 and Year 2. Added urinalysis to Day 4, Day 14 and Day 34/Day 430 Visits. • For safety monitoring. Added daily visits at Days 6-10 to perform local laboratory testing and also central laboratory testing of some parameters to prevent sharing the results of sensitive clinical data. • To allow a rapid screening for signs of development of atypical hemolytic uremic syndrome (aHUS). Re-arranged laboratory tests performed during the first two weeks of the study to allow the addition of the local laboratory testing without exceeding the blood volume limits. Added 6-month visits during the long-term follow-up period, Years 3-6 were initially annual visits. • To facilitate retention and align with clinical practice. Updated the safety data from study C3391001. Added risk potentially associated with the human albumin used in the preparation of the IP solution. Changed the description of the dose from 3E14 to 2E14 and provided an explanation based on a new titer assay method.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		• To clarify the change in nomenclature and describe the reason that the 3E14 dose used in the Phase 1b study is approximately equivalent to the 2E14 dose used in Study C3391003. Changed the endpoints for time to run/walk 10 meters and time to rise from floor to 10-meter run/walk velocity and rise from floor velocity, respectively. • To appropriately include participants in the analysis who are not able to perform the activity and can be assigned a value of zero velocity. Added efficacy endpoints to assess participants in Cohort 2 after receiving fordadistrogene movaparvovec through Year 2 Week 52 and added efficacy endpoints to assess long-term efficacy. • To align the endpoints with those for the primary analysis through Week 52. Added endpoint of ankle range of motion assessment. • A clinically meaningful measure that may reflect an additional outcome of treatment. Changed the approach to control the Type I error for select secondary endpoints from the Hochberg method to a fixed-sequence. • To employ an approach that orders the endpoints by clinical relevance rather than by p-values. Added peak FVC as an exploratory endpoint.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		• Achieving a larger absolute FVC has been shown to be associated with a slower rate of decline in respiratory function in boys with DMD. Removed DXA scans and associated endpoints. • Bone mineral density and muscle mass are unlikely to change and are difficult to interpret in this age range. Removed WPAI and HRU questionnaires from the list of endpoints. Added a description of the approach to control the rate of randomization to be implemented during the initial weeks of the study. • To help the understanding and management of potential safety risks. Added a provision for eligible siblings to receive same treatment within the study as the randomized subject. • To assist with family dynamics when more than one sibling is eligible for the study and to help prevent seroconversion, and subsequent ineligibility for treatment, of a sibling if randomized to a different cohort. Change minimum dose requirement for deflazacort for inclusion in the study from 0.5 mg/kg to 0.75 mg/kg. • To account for the different steroid potency of deflazacort compared to prednisone and prednisolone. Added inclusion criterion of a minimum NSAA total score (NSAA >16 points).

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		• There is already a maximum (NSAA <30 points) to avoid a ceiling effect. The added minimum score is to mitigate the risk of young patients with low scores who could have large gains (eg, >10 points) due primarily to cognitive/developmental changes. Added inclusion criterion: "Participants/legally acceptable representatives who are willing to protect the integrity of the study data by not actively seeking sensitive clinical data (eg, CK, AST, ALT, C3, C4, NAb to AAV9) through independent laboratory tests and by not sharing trial experiences with other participants or publicly (eg, through social media)." • To minimize the potential for functional unblinding of participants. Provided additional information on IP stability in cases of interruption of infusion. Renamed Section 6.3.3 as Clinical Sensitive Data (previously named Blinding of Laboratory Results) and updated the language in that section to align with the Blinding Plan Document. Increased the dose of IV methylprednisolone on Day 1 from 1 mg/kg to 2 mg/kg; and increased the dose of oral prednisone/prednisolone from Days 1 to 15 post-IP administration from 1 mg/kg to 2 mg/kg. This change applies to Year 1 and Year 2. • To increase immunosuppression periIP administration to help reduce the risk of immune-mediated AEs. Added provision to temporally increase the daily dose glucocorticoids within the first 2 months

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		post IP administration, if necessary to treat an immune response. • To ensure participants´ safety. Allowed other oral anti-emetics apart from ondansetron. Clarified that the local label and any specific requirement must be followed in participant´s receiving eculizumab. • To comply with local requirements. Provided more specific guidance to start treatment with eculizumab. • To ensure participants´ safety and harmonize the management of cases compatible with thrombotic microangiopathy in the study. Added a requirement that participants who experience an event compatible with aHUS will be screened for a genetic predisposition to aHUS. • To obtain information that may contribute to an understanding of the risk for developing aHUS. Changed requirement that participants who receive gene therapy other than IP after Year 1 IP administration will be withdrawn from the study; those participants will not be withdrawn from the study. Updated total blood sampling volume for individual participants.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Deleted recommendation to perform post-Baseline muscle biopsy in the same arm than the Baseline muscle biopsy. • To align with procedures used in the Phase 1b C3391001 study. Added video recording during NSAA, ankle range of motion and FVC assessments. • To enable quality control of NSAA, ankle range of motion and FVC assessments. Limited assessment of FVC to participants 6 years or older at Screening and changed the endpoint of change from Baseline in %pFVC from secondary to exploratory. • Evaluating FVC in participants younger than 6 years is difficult and unreliable and an effect of treatment is unlikely to be observed at Week 52 since untreated patients are expected to have little/no change in this age range. Updated location of the description of Ambulatory Assessment Algorithm, it will be placed in the QoL & ADL Manual and not in the Functional Assessment Manual. Added a new Section to provide guidance on the management of elevated cardiac troponin-I (cTnI) values. • Clinical experience and literature are limited relative to the management of cTnI in the setting of DMD; guidance based on a prior Pfizer interventional study of 121 DMD participants is provided.

Document History		
Document	**Version Date**	**Summary of Changes and Rationale**
		Added viral vector shedding sample collection for a subset of participants. • To support clinical trial applications and Environment Risk assessments in the European Union and Japan, and regulatory filings in all regions. Added a new Section to describe the Household Immunogenicity study. • To obtain information on the potential and timing for household contacts, including siblings, to become NAb positive following treatment with gene therapy of a family member. Added a description of the analysis approach for the skills-based endpoints. • To enable a greater understanding of how these endpoints will be evaluated and interpreted. Adapted "Appendix 7: ECG findings" to reflect pediatric participants. • To align definitions of AEs noted by ECG findings with pediatric values. Provided additional instructional text where necessary. Provided clarifying text where necessary. Corrected typographical and grammatical errors. Updated SOA to reflect corrections, changes and updates to assessments.
Original protocol	22 May 2019	Not applicable (N/A)

10.18. Appendix 18: Abbreviations

The following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
αDG	α-dystroglycan
βDG	β-dystroglycan
aHUS	Atypical hemolytic uremic syndrome
AAV	adeno-associated virus
AAV9	adeno-associated virus serotype 9
Abs	Absolute
ADA	antidrug antibodies
ADL	activities of daily living
AE	adverse event
ALT	alanine aminotransferase
ANSM	National Agency for the Safety of Medicines and Health Products
AST	aspartate aminotransferase
AxMPs	auxiliary medicinal product
AV	Atrioventricular
BBS	Biospecimen Banking System
BMD	Becker muscular dystrophy
BNP	B-type natriuretic peptide
BP	blood pressure
bpm	beats per minute
BUN	blood urea nitrogen
CBCL	Child Behavior Check List
CE	clinical evaluator
CFR	Code of Federal Regulations
CGIS	Clinician Global Impression of Severity
CIOMS	Council for International Organizations of Medical Sciences
CK	creatine kinase
CO_2	carbon dioxide (bicarbonate)
COA	clinical outcomes assessments
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	coronavirus disease 2019
CRF	case report form
CRIM	cross-reactive immune material
CRO	contract research organization
CSR	clinical study report
CT	clinical trial
CTIS	Clinical Trial Information System
cTn-I	cardiac troponin I
cTn-T	cardiac troponin T
DCT	data collection tool

Abbreviation	Term
DGC	dystrophin-associated glycoprotein complex
DILI	drug-induced liver injury
DMC	data monitoring committee
DMD	Duchenne muscular dystrophy
DNA	deoxyribonucleic acid
DRE	disease-related event
EC	ethics committee
ECG	electrocardiogram
eCRF	electronic case report form
E-DMC	external data monitoring committee
EDB	exposure during breastfeeding
EDP	exposure during pregnancy
ELISpot	Enzyme-Linked ImmunoSpot
EMA	European Medicines Agency
EQ-5D-5L	EuroQol 5 Dimension 5 Level
EQ-5D-Y	EuroQol 5 Dimensions–Youth
EU	European Union
EudraCT	European Clinical Trials Database
FAS	full analysis set
FAMPH	Federal Agency for Medicines and Health Products
FDA	Food and Drug Administration
FVC	Forced Vital Capacity
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GLDH	glutamate dehydrogenase
HAV	Hepatitis A virus
HBsAg	hepatitis B surface antigen
HCVAb	hepatitis C antibody
HIPAA	Health Insurance Portability and Accountability Act
HFI	Hereditary Fructose Intolerance
HRU:CG	Healthcare Resource Utilization Questionnaire – Caregiver
IB	Investigator's brochure
ICD	informed consent document
ICH	International Council for Harmonisation
ID	Identification
IMP	investigational medicinal product
IND	investigational new drug application
INR	international normalized ratio
IP	investigational product
IRB	institutional review board
IRT	interactive response technology
ITR	Inverted terminal repeats

Abbreviation	Term
IV	intravenous
LC-MS	liquid chromatography mass spectrometry
LFT	liver function test
LGE	late gadolinium enhancement
LVEF	left ventricular ejection fraction
MenACWY	meningococcal conjugate
MenB	serogroup B meningococcal
MHP	mental health providers
MRI	magnetic resonance imaging
mRNA	messenger ribonucleic acid
msec	Millisecond
N/A	not applicable
NAb	neutralizing antibodies
NIMP	noninvestigational medicinal product
NOAEL	No Observed Adverse Effect Level
NSAA	North Star Ambulatory Assessment
NT-ProBNP	N-terminal-pro hormone B-type natriuretic peptide
O2	oxygen
OR	Odds ratio
PACL	protocol administrative change letter
PA	protocol amendment
PASS	post-authorization safety study
PCD	primary completion date
pFVC	Predicted Force Vital Capacity
PGIS:CG	Patient Global Impression of Severity
PI	principal Investigator
PK	pharmacokinetic(s)
PMDA	Pharmaceuticals and Medical Devices Agency
PODCI	Pediatric Outcomes Data Collection Instrument
PT	prothrombin time
PVC	premature ventricular contraction/complex
QoL	quality of life
qPCR	quantitative Polymerase Chain Reaction
QTc	corrected QT
QTcF	corrected QT (Fridericia method)
rAAV	Recombinant adeno-associated virus
RBC	red blood cell
RNA	ribonucleic acid
ROM	range of motion
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV2	severe acute respiratory syndrome coronavirus 2

Abbreviation	Term
SD	standard deviation
SmPC	Summary of Product Characteristics
SoA	schedule of activities
SOP	standard operating procedure
SRSD	single reference safety document
SUSAR	suspected unexpected serious adverse reaction
TBili	total bilirubin
TEAE	treatment-emergent adverse event
TG	transgene
ULN	upper limit of normal
US	United States
VAS	visual analog scale
WPAI:DMD Caregiver	Work Productivity and Activity Impairment DMD Questionnaire – Caregiver

11. REFERENCES

1 England SB, Nicholson LV, Johnson MA, et al. Very mild muscular dystrophy associated with the deletion of 46% of dystrophin. Nature. 1990 Jan 11;343(6254):180-2.

2 Hauser MA, Robinson A, Hartigan-O'Connor D et al. Analysis of Muscle Creatine Kinase Regulatory Elements in Recombinant Adenoviral Vectors. Mol therapy 2000; 2(1): 16-25.

3 Mah JK, Korngut L, Dykeman J, et al. A systematic review and meta-analysis on the epidemiology of Duchenne and Becker muscular dystrophy. Neuromuscul Disord 2014;24(6)(Jun):482-91.

4 Hoffman EP, Brown RH, Kunkel LM. Dystrophin: the protein product of the Duchenne muscular dystrophy locus. Cell 1987; 51(6):919-28.

5 Hendriksen RG, Hoogland G, Schipper S, et al. A possible role of dystrophin in neuronal excitability: a review of the current literature. Neurosci Biobehav Rev 2015;51(Apr):255-62.

6 Anh AH and Kunkel LM. The structural and functional diversity of dystrophin. Nat Genet 1993; 3(4):283-91.

7 Nicolas A, Raguénès-Nicol C, Ben Yaou R, et al; French Network of Clinical Reference Centres for Neuromuscular Diseases (CORNEMUS). Becker muscular dystrophy severity is linked to the structure of dystrophin. Hum Mol Genet. 2015 Mar 1;24(5):1267-79.

8 Yu X, Bao B, Echigoya Y, et al. Dystrophin-deficient large animal models: translational research and exon skipping. Am J Transl Res 2015; **7**(8):1314-31.

9 Petrof BJ1, Shrager JB, Stedman HH, Kelly AM, Sweeney HL. Dystrophin protects the sarcolemma from stresses developed during muscle contraction. Proc Natl Acad Sci U S A. 1993 Apr 15;90(8):3710-4.

10 Peverelli L, Testolin S, Villa L, et al. Histologic muscular history in steroid-treated and untreated patients with Duchenne dystrophy. Neurology 2015; 85(21):1886-93.

11 Ramos J, Chamberlain JS. Gene therapy for Duchenne Muscular Dystrophy. Expert Opin Orphan Drugs 2015;3(11):1255-66.

[12] Humbertclaude V1, Hamroun D, Bezzou K, et al. Motor and respiratory heterogeneity in Duchenne patients: implication for clinical trials. Eur J Paediatr Neurol. 2012 Mar;16(2):149-60. Epub 2011 Sep 15.

[13] Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care. Lancet Neurol. 2010 Feb;9(2):177-89.

[14] Kieny P, Chollet S, Delalande P, et al. Evolution of life expectancy of patients with Duchenne muscular dystrophy at AFM Yolaine de Kepper centre between 1981 and 2011. Ann Phys Rehabil Med 2013; 56(6)(Sep):443-54.

[15] Aartsma_Rus A, Ginjaar IB, Bushby K. The importance of genetic diagnosis for Duchenne muscular dystrophy. J Med Genet 2016; 53(3):145-51.

[16] Bushby K, Finkel R, Birnkrant DJ, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. Lancet Neurol. 2010 Jan;9(1):77-93.

[17] Birnkrant DJ, Bushby K, Bann CM, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018 Mar;17(3):251-267.

[18] Birnkrant DJ, Bushby K, Bann CM, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol. 2018 Apr;17(4):347-361.

[19] Birnkrant DJ, Bushby K, Bann CM, et al; DMD Care Considerations Working Group. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. Lancet Neurol. 2018 May;17(5):445-455.

[20] Bello L, Gordish-Dressman H, Morgenroth LP, et al; CINRG Investigators. Prednisone/prednisolone and deflazacort regimens in the CINRG Duchenne Natural History Study. Neurology. 2015 Sep 22;85(12):1048-55.

[21] Prednisone SmPC. https://www.medicines.org.uk/emc/product/7650/smpc. Accessed 16 April 2019.

[22] Bushby K, Finkel R, Wong B, et al; PTC124-GD-007-DMD STUDY GROUP. Ataluren treatment of patients with nonsense mutation dystrophinopathy. Muscle Nerve. 2014 Oct;50(4):477-87.

[23] Bladen CL, Salgado D, Monges S, et al. The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. Hum Mutat. 2015 Apr;36(4):395-402.

[24] PTC Press Release. https://www.prnewswire.com/news-releases/ptc-receives-refuse-to-file-letter-from-fda-for-translarna-ataluren-300224506.html. Accessed 06 November 2018.

[25] EXONDYS 51 USPI. http://www.exondys51hcp.com/sites/default/files/EXONDYS51PI.pdf. Accessed 06 November 2018.

[26] FDA News Release. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm521263.htm. Accessed 06 November 2018.

[27] Market Watch Press Release. https://www.marketwatch.com/press-release/sarepta-receives-negative-chmp-re-examination-opinion-for-eteplirsen-2018-09-21. Accessed 06 November 2018.

[28] VYONDYS 53 US Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211970s000lbl.pdf. Accessed 17 March 2021.

[29] VILTLEPSO US Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212154s000lbl.pdf. Accessed 17 March 2021.

[30] FDA News Release. FDA approves targeted treatment for rare Duchenne muscular dystrophy mutation. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation. Published: 12 August 2020. Accessed 24 November 2020.

[31] AMONDYS 45 US Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/213026lbl.pdf. Accessed 17 March 2021.

[32] FDA News Release. FDA approves targeted treatment for rare Duchenne muscular dystrophy mutation. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-targeted-treatment-rare-duchenne-muscular-dystrophy-mutation-0. Published: 25 February 2021. Accessed 26 March 2021.

[33] Fairclough RJ, Wood MJ and Davies KE. Therapy for Duchenne muscular dystrophy: renewed optimism from genetic approaches. Nat Rev Genet 2013; 14(6):373-8.

[34] Ehmsen J, Poon E, Davies K. The dystrophin-associated protein complex. J Cell Sci 2002; 115(Pt 14)(Jul):2801-3.

[35] Wang B, Li J and Xiao X. Adeno-associated virus vector carrying human mini-dystrophin genes effectively ameliorates muscular dystrophy in mdx mouse model. Proc Natl Acad Sci USA 2000; 97(25):13714-9.

[36] Athanasopoulos T, Graham IR, Foster H, Dickson G. Recombinant adeno-associated viral (rAAV) vectors as therapeutic tools for Duchenne muscular dystrophy (DMD). Gene Ther. 2004 Oct;11 Suppl 1:S109-21.

[37] Zincarelli C, Soltys S, Rengo G, et al. Analysis of AAV serotypes 1-9 mediated gene expression and tropism in mice after systemic injection. Mol Ther 2008;16(6):1073-80.

[38] Wang B, Li J, Fu FH and Xiao X. Systemic human minidystrophin gene transfer improves functions and life span of dystrophin and dystrophin/utrophin-deficient mice. J Orthop Res 2009; 27(4):421-6.

[39] Kornegay JN, Li J, Bogan JR, et al. Widespread muscle expression of an AAV9 human mini-dystrophin vector after intravenous injection in neonatal dystrophin-deficient dogs. Mol Ther 2010; 18(8)(Aug):1501-8.

[40] Wu Z, Yang H, Colosi P. Effect of genome size on AAV vector packaging. Mol Ther. 2010 Jan;18(1):80-6.

[41] Yoshimura M, Sakamoto M, Ikemoto M, et al. AAV vector-mediated microdystrophin expression in a relatively small percentage of mdx myofibers improved the mdx phenotype. Mol Ther. 2004 Nov;10(5):821-8.

[42] Watchko J, O'Day T, Wang B, et al. Adeno-associated virus vector-mediated minidystrophin gene therapy improves dystrophic muscle contractile function in mdx mice. Hum Gene Ther. 2002 Aug 10;13(12):1451-60.

[43] Foster H, Sharp PS, Athanasopoulos T, et al. Codon and mRNA sequence optimization of microdystrophin transgenes improves expression and physiological outcome in dystrophic mdx mice following AAV2/8 gene transfer. Mol Ther. 2008 Nov;16(11):1825-32.

[44] Gregorevic P, Blankinship MJ, Allen JM, Chamberlain JS. Systemic microdystrophin gene delivery improves skeletal muscle structure and function in old dystrophic mdx mice. Mol Ther. 2008 Apr;16(4):657-64.

[45] Banks GB, Gregorevic P, Allen JM, et al. Functional capacity of dystrophins carrying deletions in the N-terminal actin-binding domain. Hum Mol Genet. 2007 Sep 1;16(17):2105-13.

[46] Gregorevic P, Allen JM, Minami E, et al. rAAV6-microdystrophin preserves muscle function and extends lifespan in severely dystrophic mice. Nat Med. 2006 Jul;12(7):787-9.

[47] Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. David J Birnkrant, Katharine Bushby, Carla M Bann, Susan D Apkon, Angela Blackwell, David Brumbaugh, Laura E Case, Paula R Clemens, Stasia Hadjiyannakis, Shree Pandya, Natalie Street, Jean Tomezsko, Kathryn R Wagner, Leanne M Ward, David R Weber, for the DMD Care Considerations Working Group* Lancet 2018; 17: 251–67.

[48] Mingozzi F, High KA. Therapeutic in vivo gene transfer for genetic disease using AAV: progress and challenges. Nat Rev Genet 2011; 12:341-55.

[49] Nathwani AC, Rosales C, McIntosh J, et al. Long-term safety and efficacy following systemic administration of a self-complementary AAV vector encoding human fix pseudotyped with serotype 5 and 8 capsid proteins. Molecular Therapy 2011a;19(5):876-85.

[50] Human Albumin. FDA Prescribing Information. https://www.fda.gov/media/80280/download.

[51] Li W, Zheng Y, Zhang W, Wang Z, Xiao J, Yuan Y. Neuromuscul Disord. 2015 May;25(5):375-80. Progression and variation of fatty infiltration of the thigh muscles in Duchenne muscular dystrophy, a muscle magnetic resonance imaging study.

[52] Ciafaloni E, Fox DJ, Pandya S, et al. Delayed diagnosis in duchenne muscular dystrophy: data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet). J Pediatr 2009 Sep;155(3):380-5.

[53] Bushby K, Connor E. Clinical outcome measures for trials in Duchenne muscular dystrophy: report from International Working Group meetings. Clin Investig (Lond) 2011; 1(9):1217-35.

[54] McDonald CM, Henricson EK, Abresch RT, et al. The cooperative international neuromuscular research group Duchenne natural history study--a longitudinal investigation in the era of glucocorticoid therapy: design of protocol and the methods used. Muscle Nerve 2013; 48(1):32-54.

[55] Mercuri E, Coratti G, Messina S, Ricotti V, Baranello G, D'Amico A, Pera MC, Albamonte E, Sivo S, Mazzone ES, Arnoldi MT, Fanelli L, De Sanctis R, Romeo DM, Vita GL, Battini R, Bertini E, Muntoni F, Pane M. PLoS One. 2016 Aug 5;11(8):e0160195. doi: 10.1371/journal.pone.0160195. eCollection 2016. Revised North Star Ambulatory Assessment for Young Boys with Duchenne Muscular Dystrophy.

[56] Zambon AA, Ayyar Gupta V, Ridout D, et al. Peak functional ability and age at loss of ambulation in Duchenne muscular dystrophy. Dev Med Child Neurol. 2022;64(8):979-988. doi:10.1111/dmcn.15176

[57] Bello L, Morgenroth LP, Gordish-Dressman H, Hoffman EP, McDonald CM, Cirak S; CINRG investigators. DMD genotypes and loss of ambulation in the CINRG Duchenne Natural History Study. Neurology. 2016 Jul 26;87(4):401-9.

[58] Mayhew AG1, Cano SJ, Scott E, Eagle M, Bushby K, Manzur A, Muntoni F; North Star Clinical Network for Neuromuscular Disease. Dev Med Child Neurol. 2013 Nov;55(11):1046-52. doi: 10.1111/dmcn.12220. Epub 2013 Aug 5. Detecting meaningful change using the North Star Ambulatory Assessment in Duchenne muscular dystrophy.

[59] Scott E, Eagle M, Mayhew A, Freeman J, Main M, Sheehan J, Manzur A, Muntoni F; North Star Clinical Network for Paediatric Neuromuscular Disease. Physiother Res Int. 2012 Jun;17(2):101-9. doi: 10.1002/pri.520. Epub 2011 Sep 23. Development of a functional assessment scale for ambulatory boys with Duchenne muscular dystrophy.

[60] Mazzone ES, Messina S, Vasco G, et al. Reliability of the North Star Ambulatory Assessment in a multicentric setting. Neuromuscul Disord 2009; 19(7):458-61.

[61] De Sanctis R, Pane M, Sivo S, Ricotti V, Baranello G, Frosini S, Mazzone E, Bianco F, Fanelli L, Main M, Corlatti A, D'Amico A, Colia G, Scalise R, Palermo C, Alfonsi C, Tritto G, Romeo DM, Graziano A, Battini R, Morandi L, Bertini E, Muntoni F, Mercuri E. Neuromuscul Disord. 2015 Jan;25(1):14-8. doi: 10.1016/j.nmd.2014.09.015. Epub 2014 Oct 6. Suitability of North Star Ambulatory Assessment in young boys with Duchenne muscular dystrophy.

[62] Sampson HA, Muñoz-Furlong A, Campbell RL, et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117(2):391-397.

[63] Miller A, Enright PL. Interpretive strategies: American Thoracic Society/European Respiratory Society 2005 Guideline Gaps. Respir Care 2012: 57(1)(Jan):127-33. 2012

American Thoracic Society/European Respiratory Study Task Force: standardization of lung function testing guidelines 2005.

64 Philip H. Quanjer, Sanja Stanojevic, Tim J. Cole. MULTI-ETHNIC REFERENCE VALUES FOR SPIROMETRY FOR THE 3–95 YEAR AGE RANGE: THE GLOBAL LUNG FUNCTION 2012 EQUATIONS: Report of the Global Lung Function Initiative (GLI), ERS Task Force to establish improved Lung Function Reference Values Eur Respir J. 2012 December ; 40(6): 1324–1343.

65 Reilly MC, Zbrozek AS, Dukes EM: The validity and reproducibility of a work productivity and activity impairment measure. PharmacoEconomics. 1993;4(5):353-65