

Title Page

LONG-TERM FOLLOW-UP SAFETY AND EFFICACY STUDY IN PARTICIPANTS WITH DUCHENNE MUSCULAR DYSTROPHY WHO HAVE RECEIVED FORDADISTROGENE MOVAPARVOVEC IN A PRECEDING CLINICAL STUDY

Study Intervention Number:	Not Applicable
Study Intervention Name:	Not Applicable
US IND Number:	IND 17598
EudraCT/CTIS Number:	Not Available
ClinicalTrials.gov ID:	Not Available
Pediatric Investigational Plan Number	EMEA-002741-PIP01-20 – study not outlined within PIP Key Elements
Protocol Number:	C3391011
Phase:	3
Brief Title: Long-Term Follow-Up Study of Fordadistrogene Movaparvovec in Duchenne Muscular Dystrophy	

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Document History

Document	Version Date
Original protocol	30 Oct 2022

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1. PROTOCOL SUMMARY

1.1. Synopsis

Protocol Title: Long-Term Follow-Up Safety and Efficacy Study in Participants with Duchenne Muscular Dystrophy Who Have Received Fordadistrogene Movaparvovec in a Preceding Clinical Study

Brief Title: Long-Term Follow-Up Study of Fordadistrogene Movaparvovec in Duchenne Muscular Dystrophy.

Rationale for Study Design:

The long-term efficacy and safety of gene therapy for DMD are not known.

Long-term collection of safety data will allow for the identification and characterization of any safety signals that may not have been detected during the initial clinical trials.

From an efficacy perspective, it may be anticipated that a single dose of fordadistrogene movaparvovec will result in persistent myocyte transduction, which will in turn lead to long-term mini-dystrophin expression and improvement in/stabilization of functional measures such as the NSAA, PUL, and pulmonary function tests. On the other hand, it is possible that mini-dystrophin expression will wane over time. Likewise, the long-term effects on cardiac function need to be assessed to address both long-term safety and efficacy effects. Data collected for 15 years post-dosing, including clinical and imaging outcomes, will allow for the determination of the durability of effect of fordadistrogene movaparvovec therapy.

Objectives and Endpoints:

Objectives	Endpoints
Primary:	**Primary:**
• Characterize the long-term safety of treatment with fordadistrogene movaparvovec	• Incidence and severity of: o SAEs o AEs considered related to previous treatment with fordadistrogene movaparvovec o Clinically significant abnormalities in cardiac troponin I, echocardiogram and ECG parameters • Incidence of malignancy
Secondary:	**Secondary:**
• Characterize the long-term efficacy of treatment with fordadistrogene movaparvovec	• Change from pre-fordadistrogene movaparvovec dosing (from interventional study), or end of interventional study, or change from first collection in: o Ability to walk 10 meters unassisted o Ability to climb stairs

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Objectives	Endpoints
	○ PUL 2.0 entry score ○ NSAA total score (subset of participants) ○ Pulmonary function test parameters %pFVC and %pPEF ○ LVEF on echocardiography • Age (years) of participants when %pFVC is <30% • Age at loss of ambulation • Age at death and cause of death • Glucocorticoid use (dose and frequency)
• Characterize the long-term health-related quality of life after treatment with fordadistrogene movaparvovec	• Change from pre-fordadistrogene movaparvovec dosing (from interventional study) or change from first collection in: ○ Modified PODCI ○ UL-PROM (non-ambulatory participants only)

Brief Summary of Study Design:

This is a multi-center, international, low-interventional, long-term follow-up study that will enroll patients with DMD who have received fordadistrogene movaparvovec in any interventional Pfizer study. Approximately 250 patients will be invited to enter this study, and if enrolled will be followed for safety and efficacy for 10 years after the end of their interventional study. Post-dose follow-up in the interventional studies is about 5 years; therefore, the fordadistrogene movaparvovec total follow-up period for patients who enter and complete this study will be about 15 years.

Participants in this study will have safety and efficacy assessments performed at the investigative clinic on a yearly basis, and check-ins at least every 6 months via a telehealth visit.

Number of Participants:

Approximately 250 pediatric and adult participants will be invited to enter this study.

Study Population:

Participants must meet the following key inclusion criterion to be eligible for enrollment into the study:

1. Participants who received fordadistrogene movaparvovec in a previous Pfizer interventional study.

Study Cohorts and Duration of Study Participation

Total duration of study participation for each participant is 10 years. There are no cohorts.

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Statistical Methods

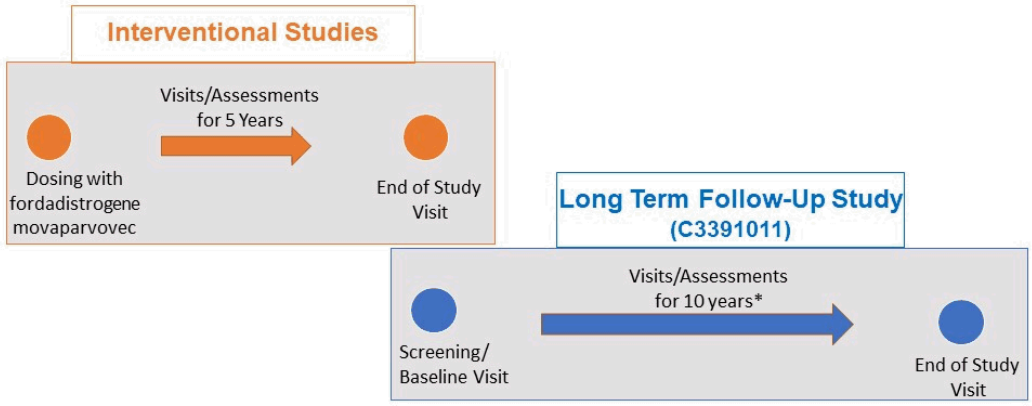
No formal hypothesis testing is planned. Data from the primary and secondary endpoints will be summarized by visit. Endpoints will be summarized by age and ambulatory status as appropriate.

There is no formal interim analysis planned for this study All available interim data from this study will be summarized and reported at the time of regulatory submission, if applicable, and subsequently will be reported through the PSUR schedule after regulatory approval.

Ethical Considerations

The risks of study participation are standard potential risks associated with blood draws, physical and neurological examinations, ECGs, echocardiograms, and pulmonary function tests. Considering the measures taken to minimize risk to participants in this study, as well as the routine nature of the study procedures and their use in standard clinical practice, the potential risks or burdens of study participation are no more than minimal. The benefits of study participation are consistent and comprehensive monitoring of the participant's health and disease status after receiving the investigational gene therapy fordadistrogene movaparvovec.

1.2. Schema



* In-clinic visits every year, with telehealth visits in between

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1.3. Schedule of Activities

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.

Tests or assessments noted as 'routine care/not required' indicate that test results must be collected in the CRF, but only if the procedure happens to be performed as part of the participant's routine healthcare. All other procedures are protocol-required.

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.

Table 1. Study Schedule of Assessments

Visit Identifier Abbreviations used in this table may be found in Section 10.9.	**Screening/ Baseline**	**3, 6, and 9 months after each annual clinic visit**	**Year 1, 2, 3, 4, 5, 6, 7, 8, 9**	**Year 10/EOS/ Early Discontinuation**	**Notes**
Visit Window	**(+12 months)**	**(± 30 days)**	**(± 45 days)**	**(± 45 days)**	Screening/ Baseline visit for this study should be conducted the same day as the End of Study visit from the interventional study (or within 12 months after that visit). See Section 8.1 for additional information.
Informed consent/assent	X				Informed consent must be obtained prior to undergoing any protocol-required tests or procedures. See Section 10.1.3 for additional information.
Review inclusion/exclusion criteria	X				See Section 5 for additional information.
Demographics	X				Includes recording previous Pfizer study number and previous Participant ID. See Section 8.1.3 for additional information.
Telehealth visit		X			Visits at 3 and 9 months after each annual clinic visit are optional, per Investigator discretion. See Section 8.1.4 for additional information.
In-clinic visit	X		X	X	See Section 8.1.4 for additional information.
Safety Assessments					
Physical examination	X		X	X	See Section 8.3.1 for additional information.

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Table 1. Study Schedule of Assessments

Visit Identifier Abbreviations used in this table may be found in Section 10.9.	**Screening/ Baseline**	**3, 6, and 9 months after each annual clinic visit**	**Year 1, 2, 3, 4, 5, 6, 7, 8, 9**	**Year 10/EOS/ Early Discontinuation**	**Notes** Screening/ Baseline visit for this study should be conducted the same day as the End of Study visit from the interventional study (or within 12 months after that visit). See Section 8.1 for additional information.
Visit Window	**(+12 months)**	**(± 30 days)**	**(± 45 days)**	**(± 45 days)**	
Neurological examination	X		X	X	See Section 8.3.2 for additional information
Weight and Height	X		X	X	See Section 8.1.1 for additional information.
Vital signs	X		X	X	Includes BP, respiratory rate, PR, and body temperature. See Section 8.3.3 for additional information.
12-Lead ECG	X		X	X	See Section 8.3.4 for additional information.
Echocardiogram	X		X	X	See Section 8.3.5 for additional information.
Cardiac MRI	X	X	X	X	Not required; data collected if performed under routine care. See Section 8.3.7 for additional information.
Laboratory Assessments					
Hematology, blood chemistry, urinalysis, cardiac troponin I	X		X	X	See Section 8.3.6 for additional information. See Section 10.2 for a list of Clinical Laboratory tests to be done. For sample collection procedures see the laboratory manual.
Retained research sample for biomarkers	X		X	X	See Section 8.5.1 for additional information
AEs and Con Meds					
Record concomitant treatment(s)	X	X	X	X	See Section 8.1.2 for additional information.
Serious and nonserious AE monitoring	X	X	X	X	See Section 8.4 for additional information.

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Table 1. Study Schedule of Assessments

Visit Identifier Abbreviations used in this table may be found in Section 10.9.	**Screening/ Baseline**	**3, 6, and 9 months after each annual clinic visit**	**Year 1, 2, 3, 4, 5, 6, 7, 8, 9**	**Year 10/EOS/ Early Discontinuation**	**Notes** Screening/ Baseline visit for this study should be conducted the same day as the End of Study visit from the interventional study (or within 12 months after that visit). See Section 8.1 for additional information.
Visit Window	**(+12 months)**	**(± 30 days)**	**(± 45 days)**	**(± 45 days)**	
Efficacy Assessments					
PUL 2.0 Entry Item	X		X	X	See Section 8.2.1 for additional information.
Pulmonary Function Tests	X		X	X	See Section 8.2.2 for additional information.
Ambulatory Status	X		X	X	See Section 8.2.3 for additional information.
Ability to Climb Stairs	X		X	X	See Section 8.2.4 for additional information.
NSAA	X	X	X	X	Only required for ambulatory participants entering from study C3391001, and only required on visits at Year 1, 2, 3, 4, and 5. For all other participants and visits, data will be collected only if performed under routine care. See Section 8.2.5 for additional information.
CGIS	X		X		Only required for ambulatory participants entering from study C3391001 who had NSAA conducted at Years 1-5. See Section 8.2.6.2 for additional information.
UL-PROM, UL-PROM-CG	X		X	X	UL-PROM is required only for non-ambulatory participants See Section 8.2.6.1 for additional information.
PODCI	X		X	X	See Section 8.2.6.3 for additional information.

2. INTRODUCTION

Fordadistrogene movaparvovec was administered to participants with Duchenne Muscular Dystrophy (DMD) prior to enrolling in this study for long-term follow-up.

Fordadistrogene movaparvovec is an AAV9 vector expressing a codon-optimized, miniaturized version of the dystrophin gene (mini-dystrophin) that encodes the domains minimally required for functionality of the dystrophin protein. It is in development as a disease modifying treatment/gene replacement therapy for DMD that will potentially slow or halt disease progression, (ie, motor and respiratory function) and/or normalize developmental milestones, regardless of underlying mutation.

2.1. Study Rationale

The purpose of the study is to collect data to characterize the long-term safety and efficacy of the investigational gene therapy fordadistrogene movaparvovec in DMD patients who have participated in a previous interventional study.

2.2. Background

DMD is the most frequently inherited pediatric neuromuscular disease and is caused by frame shift mutations in the dystrophin gene, which result in significantly reduced or absent dystrophin protein in skeletal and cardiac muscle[1,2]. The lack of functional dystrophin protein in DMD boys leads to degeneration of skeletal muscle, and ultimately heart and respiratory muscle, causing premature death[3]. There is no specific approved treatment that can stop or reverse the progression of DMD. Glucocorticoid therapy (prednisone, prednisolone, and deflazacort) has been used as the standard of care for several years.

2.2.1. Clinical Overview

There are 4 ongoing or planned interventional studies evaluating fordadistrogene movaparvovec for the treatment of DMD:

- C3391001 is a Phase 1b, first-in-human, open-label, single ascending dose study in ambulatory and non-ambulatory patients with DMD (enrollment completed).
- C3391003 is a Phase 3, global, multi-center, randomized, double blind, placebo-controlled study in ambulatory DMD patients.
- C3391008 is a Phase 2, global, multicenter, open label, study in patients with early stage DMD.
- C3391002 is a Phase 3, global, multicenter, randomized, double blind, placebo-controlled study in non-ambulatory DMD patients.

Preliminary efficacy data from Phase 1 study C3391001 includes data from 19 ambulatory participants compared to data from an external control cohort of a similar patient population (n=60). Participants who received fordadistrogene movaparvovec demonstrated an improvement in NSAA total score at 1-year, which was significantly

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different from the decline in function observed in the external control cohort. Mean (SD) change from baseline was 0.9 (4.0) for the C3391001 participants compared to -4.4 (5.3) for the external control cohort ($p<0.001$). Additionally, there was a consistent trend towards maintenance or improvement in other exploratory measures of ambulatory, upper limb, and respiratory function in the C3391001 participants compared to the external cohort[4].

Please refer to the Investigator Brochure for more detailed and updated information about safety and efficacy in the fordadistrogene movaparvovec clinical studies.

2.3. Benefit/Risk Assessment

The risks of study participation are standard potential risks associated with blood draws, physical and neurological examinations, ECGs, echocardiograms, and pulmonary function tests. Considering the measures taken to minimize risk to participants in this study, as well as the routine nature of the study procedures and their use in standard clinical practice, the potential risks or burdens of study participation are no more than minimal. The benefits of study participation are consistent and comprehensive monitoring of the participant's health and disease status after receiving the investigational gene therapy fordadistrogene movaparvovec.

The single reference safety document (SRSD) for this study is the fordadistrogene movaparvovec Investigator's Brochure, which contains full information about the known and expected benefits and risks and reasonably expected AEs of fordadistrogene movaparvovec.

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3. RESEARCH QUESTIONS, OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary:	**Primary:**
• Characterize the long-term safety of treatment with fordadistrogene movaparvovec	• Incidence and severity of: o SAEs o AEs considered related to previous treatment with fordadistrogene movaparvovec o Clinically significant abnormalities in cardiac troponin I, echocardiogram and ECG parameters • Incidence of malignancy
Secondary:	**Secondary:**
• Characterize the long-term efficacy of treatment with fordadistrogene movaparvovec	• Change from pre-fordadistrogene movaparvovec dosing (from interventional study), or end of interventional study, or change from first collection in: o Ability to walk 10 meters unassisted o Ability to climb stairs o PUL 2.0 entry score o NSAA total score (subset of participants) o Pulmonary function test parameters %pFVC and %pPEF o LVEF on echocardiography • Age (years) of participants when %pFVC is <30% • Age at loss of ambulation • Age at death and cause of death • Glucocorticoid use (dose and frequency)
• Characterize the long-term health-related quality of life after treatment with fordadistrogene movaparvovec	• Change from pre-fordadistrogene movaparvovec dosing (from interventional study) or change from first collection in: o Modified PODCI o UL-PROM (non-ambulatory participants only)

4. STUDY DESIGN

4.1. Overall Design

This is a multi-center, international, low-interventional, long-term follow-up study that will enroll patients with DMD who have received fordadistrogene movaparvovec in any interventional Pfizer study. Approximately 250 patients will be invited to enter this study, and if enrolled will be followed for safety and efficacy for 10 years after the end of their interventional study. Post-dose follow-up in the interventional studies is about 5 years; therefore, the fordadistrogene movaparvovec total follow-up period for patients who enter and complete this study will be about 15 years.

Participants in this study will have safety and efficacy assessments performed at the investigative clinic on a yearly basis, and check-ins at least every 6 months via a telehealth visit.

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4.2. Scientific Rationale for Study Design

The long-term efficacy and safety of gene therapy for DMD are not known.

Long-term collection of safety data will allow for the identification and characterization of any safety signals that may not have been detected during the initial clinical trials. As the adverse events reported in this study will be temporally far removed from the initial dosing, collection of safety data will focus on those events that are related to the gene therapy, including AEs considered to be treatment-related and clinically significant abnormalities in echocardiogram, ECG, and cardiac troponin I results. Although the recombinant AAV vector used in the fordadistrogene movaparvovec clinical program is non-integrative, and therefore not expected to be carcinogenic, malignancies will be tracked in study participants and the incidence will be determined.

From an efficacy perspective, it may be anticipated that a single dose of fordadistrogene movaparvovec will result in persistent myocyte transduction, which will in turn lead to long-term mini-dystrophin expression and improvement in/stabilization of functional measures such as the NSAA, PUL, and pulmonary function tests. On the other hand, it is possible that mini-dystrophin expression will wane over time. Likewise, the long-term effects on cardiac function need to be assessed to address both long-term safety and efficacy effects. Data collected for 15 years post-dosing, including clinical and imaging outcomes, will allow for the determination of the durability of effect of fordadistrogene movaparvovec therapy.

4.2.1. Strengths and Limitations of the Study Design and Methods

Designed as a primary data collection study, this study will provide long-term follow-up data for DMD patients who have received gene therapy. However, the analysis and interpretation of that data may be limited due to the lack of availability of natural history data for comparison at this time.

4.2.2. Patient Input Into Design

Activities with the DMD community and advocacy groups have been ongoing throughout the life of the fordadistrogene movaparvovec program (approximately 3 years) with regard to the perception of benefit/risk associated with DMD gene therapy, study design, patient reported outcomes, clinical endpoints, potential impact of the studies on patients' everyday life and their families, and factors that would influence recruitment & retention.

This ongoing outreach and collaboration between Pfizer and the DMD community will add this study to future discussions and any resulting patient input into the design of this study will be reflected here.

More frequent telehealth visits were added to the SoA based on feedback from the DMD community.

4.3. End of Study Definition

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

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A participant is considered to have completed the study if they have completed all visits of the study up to and including the Year 10/EOS visit.

5. STUDY POPULATION

The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate.

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. Participants who received fordadistrogene movaparvovec in a previous Pfizer interventional study.

5.2. Exclusion Criteria

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

1. Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members.

5.3. Lifestyle Considerations

No restrictions are required.

5.4. Screen Failures

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

Individuals who do not meet the criteria for participation in this study (screen failure) may not be rescreened.

6. STUDY INTERVENTIONS

6.1. Study Intervention(s)

In this study, there are no therapeutic study interventions, however the study does involve protocol-required diagnostic or monitoring procedures (interventions) that are considered to be minimal risk or burden to the study participant.

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6.1.1. Diagnostic or Monitoring Study Interventions

The protocol-required, non-therapeutic procedures that are considered study interventions in this study include:

- Blood draws
- Physical and neurological examinations
- ECGs
- Echocardiograms
- Pulmonary function tests
- NSAA (required for a subset of patients as described in Section 8.2.5

Refer to the SoA (Section 1.3) for the schedule and number of each of these procedures.

7. PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM STUDY

A participant may withdraw from the study at any time at their own request. Reasons for discontinuation from the study include the following:

- AE
- Death
- Lost to follow-up
- Other
- Unable to comply with the protocol
- Physician decision
- Study terminated by sponsor
- Withdrawal by Participant
- Withdrawal by Parent/Guardian

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 and then are prematurely withdrawn from the study. Participants should be questioned regarding their reason for withdrawal.

If a participant withdraws from the study, the participant 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 7.1) for disclosure of future information, no further evaluations will be performed and no additional

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data will be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent

7.1. Withdrawal of Consent

Participants who request to discontinue attending in-clinic study visits will be asked to consent to annual telehealth visits for any protocol-specified procedures that can be conducted remotely. The only exception to this is when a participant specifically withdraws consent/assent for any further contact with him or persons previously authorized by the participant to provide this information. Participants 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. The record should include whether the withdrawal only relates to attendance of in-clinic study visits or if it also represents withdrawal from telehealth visits. 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.

7.2. Lost to Follow-up

Participants will be considered lost to follow-up if they repeatedly fail to attend scheduled visits and are unable to be contacted by the study site.

The following actions must be taken if a participant fails to attend 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, then the participant will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative and Baseline Procedures

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

Participant ID numbers will be assigned sequentially by the Investigative site; ie, 4-digit assigned site number plus 4-digit subject number starting with 1001.

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Study procedures and their timing are summarized in the SoA. Protocol waivers or exemptions are not allowed. Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

The Screening/ Baseline visit for this study should be conducted the same day as the End of Study visit from the interventional study, but may be conducted up to 12 months after the End of Study visit for the interventional study. Data from the assessments performed for the last visit of the interventional study may be used for the Screening/baseline visit of this study if they were performed within 4 weeks of signing consent for this study. If the Screening/Baseline visit is conducted within 4 weeks of the End of Study visit for the interventional study, study procedures will be performed only once per participant, and the protocol-specified data will be entered in the CRF for each study. If the assessments required at the Screening/ Baseline visit for this study were not conducted in the interventional study, then they must be performed for this study.

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.

Procedures conducted as part of the participant's routine clinical management (eg, blood count) and obtained before signing of the ICD may be utilized for screening or baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the SoA.

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 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 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.

There may be instances when copies of medical records may be requested by Pfizer. In this case, all participant identifiers, with the exception of the participant number, must be redacted on the copies of medical records before submission to Pfizer.

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 180 mL. Additional blood samples may be taken for safety assessments at times specified by Pfizer, provided the total volume taken does not exceed:

- 1% of the participant's estimated total blood volume at any single time

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- 3% of the participant's estimated total blood volume during any period of 4 consecutive weeks.

8.1.1. Weight and Height Assessments

For participants who are non-ambulatory, or are not able to stand, or have contractures that prevent standing with heels on the ground, height will be calculated from the ulna length measurement. Ulna length will be measured using a segmometer. Height estimation from ulna length will follow the method developed by Gauld[5]. The estimated height will be used in the calculation for Pulmonary Function Test parameters required per Section 8.2.2.

Further instructions for height and ulna measurements are located in the Study Assessment Manual.

Body weight may be measured using a calibrated digital chair, chair scale, bed scale, wheelchair scale, or other method deemed appropriate by Investigator depending on the participant's mobility status.

8.1.2. Concomitant Therapy

Any medications that the participant is taking from the time of Screening for this study until the end of this study that are taken for DMD or its comorbidities should be captured in the CRF, including use and dose of glucocorticoids. Changes in doses of medications should also be captured.

8.1.3. Demographics

Demographics should include study number of the interventional study and participant ID from the interventional study. Race, ethnicity, and sex should be collected in compliance with local regulations.

The full date of birth (month, day, year) will be collected to critically evaluate the safety and efficacy profile by age.

8.1.4. Telehealth Visits

Telehealth visits may be used to assess participant safety and collect data points at the timepoints and for the assessments indicated in the SoA.

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 staff to communicate on aspects of clinical care, including medical advice, reminders, education, and safety monitoring. Study participants must be reminded to promptly notify site staff about any change in their health status.

Visits indicated as telehealth visits in the SoA may be done in the clinic at the discretion of the Investigator. Additionally, if a participant is unable or refuses to attend any annual, in-clinic visit(s) as indicated in the SoA, a telehealth visit may be conducted to collect any data

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(indicated in the SoA for that visit) that can be obtained remotely, as long as the participant consents (See Section 7.1).

8.2. Efficacy Assessments

8.2.1. Performance of the Upper Limb (PUL) 2.0 Entry Item

The PUL 2.0 has been demonstrated to detect progression of the upper limb involvement[6]. The entry item on the PUL 2.0 assesses the use of arms and hands on a scale of 0-6, with 6 indicating full function.

Details regarding the administration and scoring of the PUL 2.0 Entry Item are located in the Study Assessment Manual.

8.2.2. Pulmonary Function Tests

For participants aged ≥6 years, spirometry will be performed to measure FVC and PEF using standardized equipment in accordance with the modified American Thoracic Society Criteria for Acceptability for Spirometry that are specific to the DMD population[7] Sufficient forced expiratory maneuvers (up to a maximum of 10) will be performed to produce at least 3 technically adequate tracings each for FVC and PEF [8]. The best (largest) FVC and PEF measurement from each set of 3 will be determined and will be used to calculate %pFVC and %pPEF according to age, height, race, and gender using multi-ethnic reference values for spirometry for the 3–95-year age range as published by the Global Lung Function Initiative Network[9] (for %pFVC) and NHANES III Reference Values[10] (for %pPEF). For some participants, height may be calculated from the ulna length measurements per Section 8.1.1.

Whenever possible, the same clinical evaluator should administer the spirometry test for the same participant throughout the study.

Further instructions for conducting the PFTs are located in the Study Assessment Manual.

8.2.3. Ambulatory Status

Participants will be asked to walk 10 meters unassisted. Investigator staff will enter Yes or No depending on whether the participant was able to perform this task or not.

Further instructions for this assessment are located in the Study Assessment Manual.

8.2.4. Ability to Climb Stairs

Participants will be asked if they are able to climb 1 flight of stairs. Investigator staff will enter Yes or No depending on the participant response.

8.2.5. North Star Ambulatory Assessment (NSAA)

The NSAA is only required for ambulatory participants from interventional study C3391001 for Years 1-5, as indicated in the SoA. For all other participants and visits, data will be collected only if the NSAA is performed under routine care.

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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[11]). 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 2 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 (according to Section 8.2.3), then this should be reflected in scoring of the NSAA.

Clinical evaluator (CE) certification and training requirements are detailed in the NSAA manual. 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 NSAA manual.

8.2.6. Clinical Outcome Assessments

The UL-PROM will be completed for non-ambulatory participants only.

The CGIS will only be completed for participants entering from lead-in study C3391001 on the NSAA visits.

The PODCI will be completed for all participants.

Data from all clinical outcome assessments will be entered in the CRF.

8.2.6.1. DMD Upper Limb Function Patient Reported Outcome Measure (UL-PROM and UL-PROM-CG)

Non-ambulatory participants ≥17 years of age will complete the UL-PROM. Otherwise, the UL-PROM-CG version will be completed by the caregiver. Non-ambulatory participants ≥17 years of age who are physically unable to complete the UL-PROM themselves (eg, due to their disease state) may have the UL-PROM populated by an accompanying adult or site staff, based on the participant's verbal response.

The UL-PROM was developed based on FDA guidelines[12] to assess activities of daily living in DMD patients that cannot be observed in a clinical setting. The 32-item questionnaire covers 4 domains: food, self-care, household and environment, and leisure and communication. There are 3 possible response options for each item: 2 - "can do easily," 1 - "can do with difficulty," and 0 - "impossible without help." The UL-PROM total score is calculated as the sum of the individual item responses and ranges from 0 to 64, with higher scores indicating better function. The total score will be standardized to a score range of 0-100 by multiplying by 100 and dividing by 64.

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8.2.6.2. Clinician Global Impression of Severity-Ambulatory Motor Function (CGIS)

The CGIS will only be performed for the participants entering this study from study C3391001 who have had the NSAA performed in Years 1-5 according to the SoA. The CGIS is collected to enable an anchor-based method for interpreting changes in the NSAA total score and Modified PODCI scale scores. Whenever possible, the same CE who administered the NSAA should also administer the CGIS for the same participant.

The CGIS is a CE-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".

8.2.6.3. Modified Pediatric Outcomes Data Collection Instrument (PODCI; Pediatric Parent and Adolescent Versions)

The Pediatric Parent version will be completed by caregivers of all participants. Participants ≥11 years of age will complete the Adolescent version.

PODCI questionnaire scales will evaluate participants' musculoskeletal health status.

The Modified PODCI – Pediatric Parent version 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 scales each produce an independent, standardized score ranging from 0-100, with lower scores representing lower levels of function.

The Modified PODCI – Adolescent version 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).

8.3. Safety Assessments

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

8.3.1. 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, nose, mouth, skin, heart and lung, lymph nodes, gastrointestinal, and musculoskeletal systems.

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

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Physical examination findings collected during the study will be considered source data and will not be required to be reported, unless otherwise noted. Any untoward physical examination findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 3) must be reported according to the processes in Section 8.4.1 to Section 8.4.3.

8.3.2. Neurological Examination

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.

8.3.3. Vital Signs

Vital signs will be conducted before any blood collection and will include blood pressure (supine or sitting), respiratory rate, pulse rate, and body temperature.

Blood pressure and pulse rate are to be assessed after at least 5 minutes of rest using an automated device or manual technique.

Any untoward vital sign findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 3) must be reported according to the processes in Section 8.4.1 to Section 8.4.3

Temperature and respiratory rate findings collected during the study will be considered source records and will not be required to be reported, unless otherwise noted.

8.3.4. Electrocardiograms

Standard 12-lead ECGs utilizing limb leads (with a 10-second rhythm strip) should be collected at times specified in the SoA section of this protocol using an ECG machine that automatically calculates the HR and measures PR interval, QT interval, QTcF, and QRS complex. Alternative lead placement methodology using torso leads (eg, Mason-Likar) should not be used given the potential risk of discrepancies with ECGs acquired using standard limb lead placement. All scheduled ECGs should be performed after the participant has rested quietly for at least 10 minutes in a supine or sitting position.

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

In some cases, it may be appropriate to repeat abnormal ECGs to rule out improper lead placement as contributing to the ECG abnormality. It is important that leads be placed in the same positions each time in order to achieve precise ECG recordings. If a machine-read QTc value is prolonged, as defined above, repeat measurements may not be necessary if a

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qualified medical provider's interpretation determines that the QTcF values are in the acceptable range.

ECG values of potential clinical concern are listed in Section 10.7 .

8.3.5. Echocardiogram

Echocardiograms should be performed using a 2-D imaging collection method, and will be collected and read locally for interpretation and safety monitoring. A qualified individual at the investigator site will evaluate the echocardiogram for at least the left ventricular ejection fraction (LVEF), but other parameters may also be assessed, including but not limited to myocardial strain.

Echocardiogram images must be made available to a central vendor, if requested by the Sponsor, for potential central imaging reading for data analysis.

8.3.6. Clinical Safety Laboratory Assessments

See Appendix 2 for the list of clinical safety laboratory data to be collected and the SoA for the timing and frequency of laboratory data collection. The laboratory assessments must be conducted in accordance with the laboratory manual.

The investigator must review the laboratory report, document this review and record any clinically significant 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 a clinically significantly abnormal value during the study should be repeated until the value returns to normal (or baseline) or is 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.

See Appendix 5 for suggested actions and follow-up assessments in the event of potential drug-induced liver injury.

See Appendix 6 for kidney safety monitoring guidelines.

8.3.7. Cardiac MRI

Cardiac MRI is not required to be conducted for this study. However, if it is conducted for the patient's standard care of treatment at any time while enrolled in this study, its data will be entered in the CRF for this study. Data to be entered will be specified in the CRF Completion Guidelines.

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8.4. Adverse Events, Serious AEs and Other Safety Reporting

"Product under study" refers to the drug, vaccine or therapeutic device product (or any active comparator) that is the focus of the study objectives.

The definitions of an AE, SAE and Research Related Injury (RRI) can be found in Appendix 3. The investigator is required to assess whether any AE may be related to participation in the study.

All AEs (ie, serious and non-serious, including those attributed to a protocol-required procedure identified as a RRI) are collected in the clinical study database.

Should a participant, in the investigator's opinion, suffer a medically important RRI caused by their participation in the study, then the designated Pfizer clinician or medical monitor must be notified immediately by telephone or email.

AEs may arise from symptoms or other complaints reported to the Investigator by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative) or they may arise from clinical findings of the Investigator or other HCPs (clinical signs, test results, etc.).

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 the event meets the criteria for classification as an SAE or caused the participant to discontinue the study (see Section 7.1.).

During the active collection period (see Section 8.4.1), each participant and/or parent/legal guardian/legally authorized representative will be questioned about the occurrence of AEs in a nonleading manner.

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

8.4.1. Time Period and Frequency for Collecting AE and SAE Information ("Active Collection Period")

AEs and SAEs, as listed in Section 10.3.3.1, must be actively elicited and collected from each participant beginning at the time the participant or parent/legal guardian/legally authorized representative provides informed consent and ending at the end of the study (ie, the final visit or Year 10). Refer to Section 10.3.3.1 for a description of AE/SAE recording and reporting requirements for this study.

Active collection of AEs and SAEs is required whenever a protocol-required procedure is performed in the clinic on a study participant, as described here. This requirement does not apply to procedures performed as part of a participant's routine medical care (ie, procedures that are not protocol-required). Active collection of AEs and SAEs for each in-clinic,

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protocol-required procedure will start when each required procedure begins and will continue until the minimum observation period for that procedure has concluded, according to Table 2. When more than 1 protocol-required procedure is performed on a given day, the active collection period for that day will begin when the first protocol-required procedure begins and will end when observation of the last protocol-required procedure for that day has concluded. Outside of the Post-Procedure Observation Periods, only targeted AEs, as listed in Section 10.3.3.1, will be captured.

Table 2. Procedure-Observation Timetable

Procedure	Minimum Observation Time (after the procedure has concluded)
Physical & Neurological Exam	30 minutes
Weight & Height	30 minutes
Vital Signs	30 minutes
ECG	2 hours
Echocardiogram	2 hours
Blood samples	2 hours
Urine samples	15 minutes
PUL, Ambulatory Status, Ability to Climb Stairs	2 hours
NSAA	2 hours
Clinical Outcome Assessments	1 hour

Follow-up by the investigator continues throughout the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

When a clinically important AE remains ongoing at the end of the active collection period, then follow-up by the investigator continues until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator and Pfizer concurs with that assessment.

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

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.

Investigators are not obligated to actively solicit AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has completed the study, and they consider the event to

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be reasonably related to the product under study, the investigator must promptly report the SAE to Pfizer using the CT SAE Report Form.

8.4.1.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period as described in Section 8.4.1, are reported to Pfizer Safety on the CT SAE Report Form immediately upon awareness 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.

8.4.1.2. Recording Nonserious AEs and SAEs on the CRF

All SAEs and non-serious AEs and SAEs occurring during the active collection period (see Section 8.4.1) must be recorded in the AE section of the CRF.

The investigator is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs.

As part of ongoing safety reviews conducted by the sponsor, any non-serious AE that is determined by the sponsor to be serious will be reported by the sponsor as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

8.4.2. 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 must 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.

8.4.3. 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 the event has resolved, stabilizes or is otherwise explained, or the participant has been lost to follow-up (as defined in Section 7.2).

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 provided in Appendix 3.

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8.4.4. 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 toward the safety of participants and the safety of the product 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 the product under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

8.4.5. Exposure During Pregnancy or Breastfeeding, and Environmental/Occupational Exposure

The requirements for reporting exposure during pregnancy or breastfeeding and environmental exposure (including occupational exposure) apply throughout the entire active collection period and are outlined below; when such reports are required per protocol, the report must be transmitted to Pfizer Safety within 24 hours of investigator awareness.

8.4.5.1. Exposure During Pregnancy

An EDP occurs if:

- A male participant who has received fordadistrogene movaparvovec in a previous study inseminates a female partner.

- A male participant uses any Pfizer medicinal product under routine care, during the study period (eg, a concomitant medication marketed by Pfizer) and his partner subsequently becomes pregnant; or,

The investigator must report the EDP to Pfizer Safety within 24 hours of the investigator's awareness of the EDP, whether or not an SAE has occurred.

- The initial information submitted should include the anticipated delivery date of the baby (see below for information related to termination of pregnancy).

- An EDP report is not required if the Pfizer product taken under routine care is specifically approved for use in pregnant women (eg, vitamins) and is administered in accord with authorized use. However, if the infant experiences an SAE associated with such a drug, the SAE must be reported along with the EDP.

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The Investigator must report the EDP to Pfizer Safety on the CT SAE Report Form and the EDP Supplemental Form.

Relevant details of the exposure and the pregnancy will be collected from the time informed consent was provided until final study follow-up. If there is an SAE associated with the EDP, then the SAE is reported to Pfizer Safety using the CT SAE Report Form.

Follow-up must be conducted to obtain general information on the pregnancy and its outcome for all EDP reports. 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. For a live birth, information regarding the structural integrity of the neonate at the time of birth should be provided. In the event of a termination, the reason(s) for termination should be provided and information regarding the structural integrity of the terminated fetus should be included in the report (if available; not required if pre-procedure test findings were conclusive for a congenital anomaly and those findings are provided in the report).

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), then the investigator should follow the procedures for reporting SAEs.

Pregnancy outcomes that are reported to Pfizer Safety as SAEs include:

- 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 as SAEs, without regard to causality.
- 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 product under study.

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 may be requested 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.

8.4.5.2. Exposure during Breastfeeding

Not Applicable

8.4.5.3. Environmental/Occupational Exposure

Not Applicable

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8.4.6. Cardiovascular and Death Events

Collected as part of protocol-required safety monitoring.

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

Not applicable

8.4.8. Adverse Events of Special Interest

Not applicable

8.4.8.1. Lack of Efficacy

In this study, lack of efficacy is defined in terms of any approved Pfizer medicinal product used by the participant under routine care (ie, used as a concomitant medication) and is reportable to Pfizer Safety if the Investigator is made aware of the lack of efficacy.

Lack of efficacy is the failure of expected pharmacologic action or therapeutic benefit.

If the lack of efficacy involves a Pfizer vaccine, contraceptive or product that is used in the treatment of life-threatening diseases or conditions (eg, anti-infectives), excluding HIV and cancer, the lack of efficacy should be reported to Pfizer Safety (as an SAE). For all other Pfizer products, lack of efficacy is reportable to Pfizer Safety only if an SAE occurs in association with the lack of efficacy.

8.4.9. Medical Device Deficiencies

Not applicable

8.4.10. Medication Errors

Medication errors may result from the administration or consumption of a Pfizer drug or vaccine product by the wrong participant; at the wrong time; at the wrong dosage or strength; etc.

Any medication error that (a) involves the use of an approved Pfizer product taken by the participant as part of their routine healthcare and (b) is associated with a SAE must be reported to Pfizer Safety within 24 hours of the Investigator's awareness using the CT SAE Report Form (see Section 8.4.1.1).

8.5. Biomarkers

8.5.1. Retained Research Samples for Biomarkers

These retained research samples will be collected in this study:

- 4-mL whole blood; Prep B2.5 (to be aliquoted into 4 x 0.5 mL serum samples)
- 2-mL whole blood; Prep B1.5 optimized for plasma

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Retained research samples will be collected as local regulations and IRB/ECs allow according to the SoA, if limits on blood volume collection have not been exceeded.

Retained Research Samples may be used for research related to the investigational therapy fordadistrogene movaparvovec and DMD. Genes and other analytes (eg, proteins, RNA, nondrug metabolites) may be studied using the retained samples.

See Section 10.4 for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in the central laboratory manual.

9. STATISTICAL CONSIDERATIONS

9.1. Statistical Hypotheses

No formal hypothesis testing will be conducted. Data from the primary and secondary endpoints will be summarized by visit. Endpoints will be summarized by age and ambulatory status as appropriate.

9.2. Sample Size Determination

Sample size is based on the number of participants enrolled in C339 interventional clinical trials and is anticipated to be ~250 participants.

9.3. Data Management

A Pfizer database will be used, and Pfizer will be responsible for the data management of this study, including quality checking of the data. Details are included in the Data Management Plan.

9.4. Case Report Forms

As used in this protocol, the term CRF refers to an electronic data record.

A CRF is required and should be completed for each included subject. The completed original CRFs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer. The investigator shall ensure that the CRFs are securely stored at the study site in encrypted electronic form and will be password protected to prevent access by unauthorized third parties.

The investigator has ultimate responsibility for the collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms (source documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The CRFs must be signed by the investigator to attest that the data contained on the CRFs are true. Any corrections to entries made in the source documents must be dated, initialed, and explained (if necessary).

In most cases the source documents are the hospital or the physician's chart. In these cases, data collected on the CRFs must match those charts.

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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.

9.5. Data Analysis

The endpoints listed in Section 3 will be summarized by age and ambulatory status as appropriate.

Detailed methodology for summary and statistical analyses of data collected in this study will be documented in a statistical analysis plan (SAP), which will be dated, filed and maintained by the sponsor. The SAP may modify the plans outlined in the protocol; any major modifications of primary endpoint definitions or their analyses would be reflected in a protocol amendment.

Pharmacogenomic or biomarker data from Retained Research Samples may be collected during or after the study and retained for future analyses; the results of such analyses are not planned to be reported.

9.6. Interim Analyses

There is no formal interim analysis planned for this study. All available interim data from this study will be summarized and reported at the time of regulatory submission, if applicable, and subsequently will be reported through the PSUR schedule after regulatory approval.

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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:

- Consensual 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, SRSD(s), and other relevant documents (e.g., 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.

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 (i.e., 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 product under study, Pfizer should be informed immediately.

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 the ICH GCP guidelines that the investigator becomes aware of.

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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

10.1.3.1. Adult Participants

The investigator or the investigator's representative will explain the nature of the study, including the risks and benefits, to the participant and answer all questions regarding the study. The participant should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

Participants must be informed that their participation is voluntary. Participants will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, privacy and data protection requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each participant is 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 must be informed that their 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.

The participant must be informed that their 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 is fully informed about their right to access and correct their personal data and to withdraw consent for the processing of their personal data.

The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date on which the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

Participants must be reconsented to the most current version of the IRB/EC-approved ICD(s) during their participation in the study as required per local regulations.

A copy of the ICD(s) must be provided to the participant.

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10.1.3.2. Pediatric Participants

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 his or her own assent, the source documents must record why the participant did not provide assent (for example, 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/IEC 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. 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

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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 his or her right to access and correct his or her child's personal data and to withdraw consent for the processing of his or her 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.

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

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 his or her actual identity and medical record identification. 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.

The contract between sponsor and study sites specifies responsibilities of the parties related to data protection, including handling of data security breaches and respective communication and cooperation of the parties.

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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 standard operating procedures on how to respond in the event of unauthorized access, use, or disclosure of sponsor information or systems.

10.1.5. Committees Structure

Safety data from this study will be shared with the established fordadistrogene movaparvovec program-level External Data Monitoring Committee (E-DMC), which evaluates unblinded safety data for ongoing clinical trials, until all interventional clinical studies have completed and the E-DMC is dissolved.

10.1.6. 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/CTIS and/or www.pfizer.com and other public registries and websites 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.

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Documents within marketing authorization packages/submissions

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 statistical analysis plans. 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 available data from these trials 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.

10.1.7. Data Quality Assurance

All participant data relating to the study will be recorded on 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 form and are password protected 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 data 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 (e.g., 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 data management plan and monitoring plan maintained and utilized by the sponsor or designee.

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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.

10.1.8. 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.

Data reported on the CRF or entered in the eCRF that are 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.

Definition of what constitutes source data and its origin can be found in the Source Document Locator, which is maintained by the sponsor.

Description of the use of the computerized system is documented in the Data Management Plan, which is maintained by the sponsor.

The investigator must maintain accurate documentation (source data) that supports the information entered in the CRF.

The sponsor or designee will perform monitoring to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being

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conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP guidelines, and all applicable regulatory requirements.

10.1.9. Study and Site Start and Closure

The study start date is the date on which the clinical study will be open for recruitment of participants.

The first act of recruitment is the date of the first participant's first visit and will be the study start date.

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 sponsor or designee 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 the ICH 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.

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

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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.

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10.2. Appendix 2: Clinical Laboratory Tests

The following protocol-required laboratory tests will be performed at times defined in the SoA. 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 by the investigator at any time during the study to assess any perceived safety issues.

Table 3. Protocol-Required Safety Laboratory Assessments

Hematology	Chemistry & Hepatic Safety	Urinalysis	Other
Hemoglobin	BUN and creatinine	pH	Cardiac troponin I
Hematocrit	Glucose (random)	Glucose (qual)	
RBC count and morphology	Calcium	Protein (qual)	
Platelet count	Sodium	Blood (qual)	
WBC count (and morphology as applicable)	Potassium	Ketones	
Neutrophils (Abs)	Chloride	Nitrates	
Eosinophils (Abs)	Total CO2 (bicarbonate)	Leukocyte esterase (qual)	
Monocytes (Abs)	Total, direct, and indirect bilirubin	Microscopy and culture[a]	
Basophils (Abs)	Alkaline phosphatase		
Lymphocytes (Abs)	Albumin		
	Creatine kinase		
	Total protein		
	Serum phosphatase		
	GGT		
	ALT, AST		
	Cystatin C		
	GLDH		

a. Only if urine dipstick is positive for blood, protein, nitrates, or leukocyte esterase.

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

In this protocol, "product under study" refers to the drug, therapeutic medical device or vaccine product (or any active comparator or placebo) that is relevant to the study objectives.

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 the product under study, whether or not considered related to the product under study.

- 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 the product under study.

Events Meeting the AE Definition

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (e.g., ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Any abnormal laboratory test results that meet any of the conditions below must be recorded as an AE:
    - Is associated with accompanying symptoms.
    - Requires additional diagnostic testing or medical/surgical intervention.
    - Leads to a change in study dosing (outside of any protocol-specified dose adjustments) or discontinuation from the study, significant additional concomitant drug treatment, or other therapy.
    - Exacerbation of a chronic or intermittent preexisting condition including an increase in frequency and/or intensity of the condition.
- New condition detected or diagnosed after administration of the product under study 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 the product under study or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

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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 (e.g., 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

An SAE is defined as any untoward medical occurrence that, at any dose, meets one or more of the following criteria:

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 admitted (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.

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.

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- This definition is not intended to include experiences of relatively minor medical significance such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle) that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Is a suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic

- The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant 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.

g. 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.

h. Research Related Injury

Should a participant, in the investigator's opinion, suffer a medically important research related injury caused by their participation in the study, the designated Pfizer clinician or medical monitor must be notified immediately by telephone or email.

A medically important research related injury is any untoward medical occurrence that:

- Results in death;
- Is life-threatening (immediate risk of death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);
- Results in congenital anomaly/birth defect.

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Medical and scientific judgment is exercised in determining whether an injury is an important medical event. An important medical event may not be immediately life-threatening and/or result in death or hospitalization. However, if it is determined that the event may jeopardize the participant or may require intervention to prevent one of the other outcomes listed in the definition above, the important medical event should be reported as a research related injury.

An investigator may be requested by the designated Pfizer clinician or medical monitor to obtain specific additional follow-up information in an expedited fashion. In general, this will include a description of the injury in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Information on other possible causes of the event, such as concomitant treatments, vaccines, and/or 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 or its designated representative.

10.3.2.1. Definition of Medication Error:

A medication error is any unintentional error in the prescribing, dispensing, or administration of a medicinal product that may cause or lead to inappropriate medication use or patient harm while in the control of the healthcare professional, patient, or consumer. Such events may be related to:

- Professional practice,
- Procedures,
- Systems, including:
  - Prescribing
  - Order communication
  - Product labeling, packaging, and nomenclature
  - Dispensing
  - Distribution
  - Administration
  - Education
  - Monitoring
  - Use

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Medication errors also include near-misses involving or not involving a patient directly or confusion regarding invented names (e.g., trade name, brand name).

10.3.2.2. Definition of Overdose

An overdose is an administration of a quantity of a medicinal product given per administration or cumulatively that is above the maximum recommended dose according to the authorized product information.

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

10.3.3.1. AE and SAE Recording/Reporting during the Active Collection Period

The table below summarizes the requirements for recording AEs on the CRF and for reporting serious AEs on the CT SAE Report Form to Pfizer Safety throughout the active collection period(s). These requirements are delineated for 3 types of events: (1) SAEs; (2) non-serious AEs (AEs); and (3) exposure to the drug product under study (or any Pfizer product used under routine care) during pregnancy or breastfeeding, or an environmental/occupational exposure to the product under study.

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	Record on the CRF	Report on the CT SAE Report Form to Pfizer Safety within 24 hours of awareness
SAEs	All SAEs occurring during the active collection period.	All SAEs occurring during the active collection period. Any SAEs (including death) that occur after the active collection period(s) and the investigator suspects may be related to the product under study
Non-serious AEs	All non-serious AEs occurring during the post-procedure observation periods. Outside of the post-procedure observation periods: • any non-serious AE that is deemed related to study drug per Investigator • any non-serious clinically significant abnormality found on echocardiogram, ECG, or cardiac troponin I • any malignancy	None

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Safety Event	Record on the CRF	Report on the CT SAE Report Form to Pfizer Safety within 24 hours of awareness
Scenarios involving exposure during pregnancy (EDP).	Instances of EDP are not captured in the CRF.	All instances of EDP for any Pfizer product used under routine care are reported (whether or not there is an associated SAE)*

*** EDP** (with or without an associated AE or SAE): any pregnancy information is reported to Pfizer Safety using the CT SAE Report form and EDP Supplemental Form; if the EDP is associated with an SAE, then the SAE is reported to Pfizer Safety using the CT SAE Report form.

When an AE/SAE occurs:

- It is the responsibility of the investigator to review all documentation (e.g., 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.

10.3.3.2. Assessment of Intensity

When required on the AE page of the CRF, the investigator will assess intensity for each AE and SAE reported during the study and assign it to one of the following categories:

- Mild: A type of AE that is usually transient and may require only minimal treatment or therapeutic intervention. The event does not generally interfere with usual ADL.
- Moderate: A type of AE that is usually alleviated with additional specific therapeutic intervention. The event interferes with usual ADL, causing discomfort, but poses no significant or permanent risk of harm to the research participant.
- Severe: A type of AE that interrupts usual ADL, or significantly affects clinical status, or may require intensive therapeutic intervention.

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Note: An event is defined as "serious" because it meets at least one of the predefined outcomes as described in the definition of an SAE - NOT because it is rated as severe.

10.3.3.3. Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE and SAE. The investigator will use clinical judgment to determine the relationship.

- 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.

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

- The investigator will also consult the IB and/or product information, for marketed products, in their assessment.

- For each AE and SAE, the investigator **must** document in the medical notes that they have reviewed the AE or SAE and 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 assess 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 if the product under study caused the event, then the event will be handled as "related to product under study" 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 in the dedicated section of the CT SAE Report Form, in accordance with the SAE reporting requirements.

10.3.3.4. Follow-up of AEs and SAEs

- The investigator is obligated to perform or arrange for the conduct of supplemental, minimal-risk 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

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possible. These may include additional laboratory tests or investigations, histopathological examinations or consultation with other healthcare providers.

- 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.

- 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 the 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, an alternative method should be used, eg, secured (Transport Layer Security) or password-protected email. If none of these methods can be used, notification by telephone is acceptable with a copy of the CT SAE Report Form is 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.

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10.4. Appendix 4: 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.

- The scope of the genetic research may be narrow (eg, 1 or more candidate genes) or broad (eg, the entire genome), as appropriate to the scientific question under investigation.

- The samples may be analyzed as part of a multistudy assessment of genetic factors involved in the response to fordadistrogene movaparvovec 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 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.

- Retained samples will be stored indefinitely or for another period as per local requirements.

- Participants may withdraw their consent for the storage and/or use of their Retained Research Samples 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.

- Samples for genetic research will be labeled with a code. The key between the code and the participant's personally identifying information (eg, name, address) will be held securely at the study site.

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10.5. Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments - Potential Cases of Drug-Induced Liver Injury

It is required that potential DILI (Hy's law) cases are to be reported to Pfizer Safety as SAEs, irrespective of the availability of full results from the investigations performed to determine the etiology of the LFT abnormalities.

Guidance: Management and Follow-up of 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 DILI. Participants who experience a transaminase elevation above 3 × ULN should be monitored more frequently to determine if they are "adaptors" or are "susceptible."

In the majority of DILI cases, elevations in AST and/or ALT precede T bili elevations (>2 × ULN) by several days or weeks. The increase in T bili typically occurs while AST/ALT is/are still elevated above 3 × ULN (i.e., AST/ALT and T bili values will be elevated within the same laboratory sample). In rare instances, by the time T bili 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 T bili 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 T bili baseline values within the normal range who subsequently present with AST OR ALT values >3 × ULN AND a T bili 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** T bili 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 T bili above the normal range: T bili level increased from baseline value by an amount of ≥1 × ULN **or** if the value reaches ≥3 × ULN (whichever is smaller).

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Rises in AST/ALT and T bili 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 T bili for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/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 should be collected that includes relevant information such as ethanol, acetaminophen/paracetamol (either by itself or as a co-formulated product in prescription or over-the-counter medications), recreational drug or supplement (herbal) use or consumption; family, sexual and travel history; history of contact with a jaundiced person; surgery; blood transfusion; history of liver or allergic disease; and potential occupational exposure to chemicals. Further testing for acute hepatitis A, B, C, D and E infection and liver imaging (e.g., biliary tract) and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and T bili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the 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.

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10.6. Appendix 6: Kidney Safety: Monitoring Guideline

10.6.1. Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury

Standard kidney safety monitoring requires assessment of baseline and postbaseline serum creatinine (serum creatinine measurement to eGFR [serum creatinine -based eGFR] or [eCrCl]). Baseline and postbaseline serum cystatin C make it feasible to distinguish acute kidney injury (AKI) from other causes of serum creatinine increase. If serum creatinine increase is confirmed after baseline, then reflex measurement of serum cystatin C is indicated to estimate the combined serum creatinine - serum cystatin C eGFR calculation (for adults only).

Regardless of whether kidney safety and function monitoring tests are required as a routine safety monitoring procedure in the study, if the investigator or Sponsor deem it necessary to further assess kidney safety and quantify kidney function, then these test results should be managed and followed per standard of care.

10.6.1.1. Grading of Clinically Relevant Decrease in Kidney Function

Pre- and post-baseline calculations to estimate kidney function (Section 10.6.2) permit assessment of change from baseline kidney function grade (G1-G5). Post-baseline, clinically relevant change in kidney function is characterized by grade shift from G1 to G2-G5, G2 to G3a-G5, G3b to G4-G5, or G4 to G5 and may necessitate temporary or permanent withdrawal of study intervention until all clinical, laboratory, and radiologic testing are completed.

GFR categories (ml/min/ 1.73 m^2) Description and range			
	G1	Normal or high	≥90
	G2	Mildly decreased	60-89
	G3a	Mildly to moderately decreased	45-59
	G3b	Moderately to severely decreased	30-44
	G4	Severely decreased	15-29
	G5	Kidney failure	<15

[KDIGO, 2013]

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10.6.1.2. Grading of Clinically Relevant Increase in Albuminuria

Clinically relevant change in albuminuria is characterized using 2012 KDIGO Guidelines categories, A1 to A3.

Persistent albuminuria categories Description and range		
A1	**A2**	**A3**
Normal to mildly increased	Moderately increased	Severely increased
<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol

[KDIGO, 2013]

Post-baseline, clinically relevant change in albuminuria (with or without eGFR decline) is defined by a shift or change in Albuminuria Grade (A1 to A2 or A3; A2 to A3).

10.6.1.3. Interpreting Post-Baseline Changes in Serum Creatinine-based Kidney Function Assessments

Participants exposed to study intervention demonstrating transient or sustained increase in serum creatinine (with decrease in serum creatinine -based eGFR or CrCL) require expeditious evaluation to differentiate AKI from drug-induced creatinine increase (DICI). DICI is defined as transporter-mediated effect related to altered renal tubular creatinine handling without histological injury.

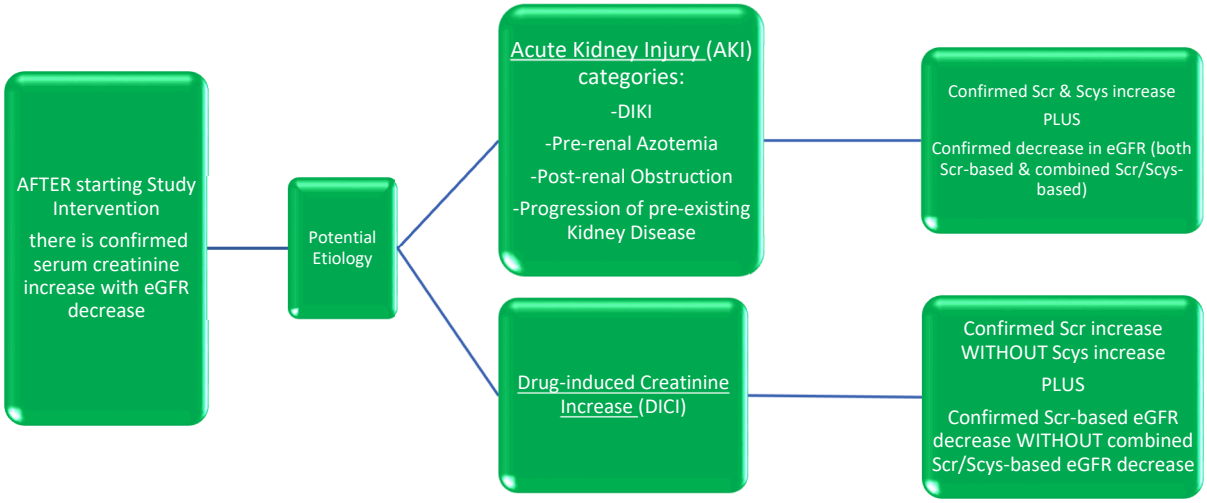
10.6.1.4. Differentiating Acute Kidney Injury (AKI) from Drug-Induced Creatinine Increase (DICI)

Both AKI and DICI are associated with (i) confirmed serum creatinine increase ≥0.3 mg/dL (≥26.5 µmol/L) within 48 hours; or (ii) confirmed serum creatinine increase ≥1.5 times baseline (known or suspected to have occurred within the prior 7 days).

AKI is associated with (i) simultaneous, confirmed serum cystatin C increase and confirmed serum creatinine increase and decrease in serum creatinine-based eGFR and combined serum creatinine - serum cystatin C -based eGFR (where applicable), (ii) confirmed albuminuria increase OR (iii) urine volume <0.5 mL/kg/h for 6 consecutive hours.

DICI is associated with confirmed serum creatinine increase WITHOUT confirmed increase in reflex serum cystatin C AND confirmed serum creatinine -based eGFR decrease WITHOUT confirmed combined serum creatinine- serum cystatin C -based eGFR decrease (where applicable).

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Confirmed post-baseline decrease in kidney function should be assessed individually based on clinical judgment. Cases wherein uncertainty remains, the Investigator can review the case with the sponsor.

The participant should return to the site for evaluation as soon as possible, preferably within 48 hours of awareness of the abnormal results. Evaluation should include physical examination, laboratory tests, detailed medical and surgical history, review of all medications (including recreational drugs and supplements [herbal]), family history, sexual history, travel history, blood transfusion, and potential occupational exposure to chemicals. If appropriate, nephrology consultation may be recommended to facilitate differentiation of renal parenchymal disease, pre-renal azotemia, and post-renal obstruction.

All confirmed cases of clinically relevant decrease in kidney function should be considered potential DIKI cases if no other reason for the kidney function abnormalities has been found.

10.6.2. Age-Specific Kidney Function Calculation Recommendations

10.6.2.1. Adults (18 years and above)—2021 CKD-EPI Equations

2021 CKD-EPI Serum creatinine only	**Serum creatinine** *(mg/dL)*	**Serum cystatin C** *(mg/L)*	**Recommended eGFR Equation**
Male	if ≤ 0.9	N/A	eGFR = 142 × (serum creatinine /0.9)$^{-0.302}$ × (0.9938)^{Age}
Male	if > 0.9	N/A	eGFR = 142 × (serum creatinine /0.9)$^{-1.200}$ × (0.9938)^{Age}
2021 CKD-EPI serum creatinine - Serum cystatin C combined	**Serum creatinine** *(mg/dL)*	**Serum cystatin C** *(mg/L)*	**Recommended eGFR Equation**
Male	if ≤ 0.9	if ≤ 0.8	eGFR = 135 × (serum creatinine /0.9)$^{-0.144}$ × (serum cystatin C/0.8)$^{-0.323}$ × (0.9961)^{Age}
Male	if ≤ 0.9	if > 0.8	eGFR = 135 × (serum creatinine /0.9)$^{-0.144}$ × (serum cystatin C /0.8)$^{-0.778}$ × (0.9961)^{Age}
Male	if > 0.9	if ≤ 0.8	eGFR = 135 × (serum creatinine /0.9)$^{-0.544}$ × (serum cystatin C /0.8)$^{-0.323}$ × (0.9961)^{Age}
Male	if > 0.9	if > 0.8	eGFR = 135 × (serum creatinine /0.9)$^{-0.544}$ × (serum cystatin C /0.8)$^{-0.778}$ × (0.9961)^{Age}

[Inker et al, 2021]

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10.6.2.2. Adolescents (12 years to <18 years)—Cockcroft-Gault Formula

Males: Cr/Cl (mL/min) = [(140 - age) × body weight (in kg)] / [serum creatinine (in mg/dL) × 72]

10.6.2.3. Children (2 years to <12 years)—Modified Schwartz Equation

CrCl normalized to body surface area (mL/min/1.73 m^2) = (K X Ht)/ serum creatinine

Height in centimeters; Serum creatinine in mg/dL.

K (proportionality constant): Male Child < 12 years: K = 0.70

10.6.3. Non-Renal Factors Impacting Serum Cystatin C Values

Cystatin C is removed from the blood solely by glomerular filtration, while creatinine is removed by glomerular filtration and renal tubular secretion. Variability in serum cystatin C levels (independent of kidney function) may occur in the following clinical scenarios:

- Hyperthyroidism (associated with increased serum cystatin C)
- Hypothyroidism (associated with decreased serum cystatin C)
- High-potency glucocorticoid (eg, dexamethasone) treatment
- Cigarette smoking
- Pregnancy
- Chronic inflammatory disease states (malignancy, HIV infection, rheumatologic diseases, autoimmune diseases, chronic viral or bacterial infection)
- Markedly elevated C-reactive protein
- Mutations/polymorphisms in the cystatin C promoter regions

10.6.4. References

Inker LA, Eneanya ND, Coresh J, et al. New creatinine- and cystatin C–based equations to estimate GFR without race. N Engl J Med. 2021; 385:1737-49.

KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.

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10.7. Appendix 7: ECG Findings of Potential Clinical Concern

ECG Findings That <u>May</u> Qualify as AEs
• Marked sinus bradycardia (rate <40 bpm) lasting minutes. • New PR interval prolongation >280 ms. • New prolongation of QTcF to >480 ms (absolute) or by ≥60 ms from baseline. • New-onset atrial flutter or fibrillation, with controlled ventricular response rate: ie, rate <120 bpm. • New-onset type I second-degree (Wenckebach) AV block of >30 seconds' duration. • Frequent PVCs, triplets, or short intervals (<30 seconds) of consecutive ventricular complexes.
ECG Findings That <u>May</u> Qualify as SAEs

• QTcF prolongation >500 ms.
• New ST-T changes suggestive of myocardial ischemia.
• New-onset LBBB (QRS complex >120 ms).
• New-onset right bundle branch block (QRS complex >120 ms).
• Symptomatic bradycardia.
• Asystole:
  • In awake, symptom-free participants in sinus rhythm, with documented periods of asystole ≥3.0 seconds or any escape rate <40 bpm, or with an escape rhythm that is below the AV node;
  • In awake, symptom-free participants with atrial fibrillation and bradycardia with 1 or more pauses of at least 5 seconds or longer;
  • Atrial flutter or fibrillation, with rapid ventricular response rate: rapid = rate >120 bpm.
• Sustained supraventricular tachycardia (rate >120 bpm) ("sustained" = short duration with relevant symptoms or lasting >1 minute).

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- Ventricular rhythms >30 seconds' duration, including idioventricular rhythm (HR <40 bpm), accelerated idioventricular rhythm (HR 40 bpm to <100 bpm), and monomorphic/polymorphic ventricular tachycardia (HR >100 bpm [such as torsades de pointes]).
- Type II second-degree (Mobitz II) AV block.
- Complete (third-degree) heart block.

ECG Findings That Qualify as SAEs

- 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.

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10.8. Appendix 8: Country-Specific Requirements

10.8.1. France Contrat Unique

This section is only for Investigative sites in France.

1. GCP Training

   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. Study Intervention

   No participants or third-party payers will be charged for study intervention.

3. Urgent Safety Measures

   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

   Pfizer retains the right to discontinue development of fordadistrogene movaparvovec at any time.

10.8.2. Germany-Specific Requirements

This section is only for Investigative sites in Germany.

The participant and/or their parent(s)/legal guardian must agree at the Screening Visit that an autopsy will be performed if the participant dies within 10 years of administration of fordadistrogene movaparvovec.

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10.9. Appendix 9: Abbreviations

The following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
AAV	adeno associated virus
AAV9	adeno associated virus serotype 9
Abs	absolute
ADL	activity/activities of daily living
AE	adverse event
AKI	acute kidney injury
ALT	alanine aminotransferase
AST	aspartate aminotransferase
AV	atrioventricular
BP	blood pressure
bpm	beats per minute
BUN	blood urea nitrogen
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
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CRF	case report form
CrCl	creatinine clearance
CRO	contract research organization
CSR	Clinical Study Report
CTIS	Clinical Trial Information System
CT SAE	Clinical Trial Serious Adverse Event
DICI	drug-induced creatinine increase
DILI	drug-induced liver injury
E-DMC	External Data Monitoring Committee
DMD	Duchenne muscular dystrophy
EC	ethics committee
ECG	electrocardiogram or electrocardiography
eCRF	electronic case report form
EDP	exposure during pregnancy
eGFR	Estimated glomerular filtration rate
EMEA	European Medicines Evaluation Agency
EOS	end of study
EU	European Union
EudraCT	European Union Drug Regulating Authorities Clinical Trials (European Clinical Trials Database)
FDA	Food and Drug Administration
FVC	Forced vital capacity

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Abbreviation	Term
GCP	Good Clinical Practice
GFR	glomerular filtration rate
GGT	gamma-glutamyl transferase
HCP	health care provider
HIPAA	Health Insurance Portability and Accountability Act
HR	heart rate
IB	Investigator's Brochure
ICD	Informed Consent Document
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ID	identification
IEC	Independent Ethics Committee
IND	Investigational New Drug
INR	international normalized ratio
IRB	Institutional Review Board
K	proportionality constant
LBBB	left bundle branch block
LFT	liver function test
LVEF	left ventricular ejection fraction
MRI	magnetic resonance imaging
N/A	not applicable
NSAA	North Star Ambulatory Assessment
PEF	peak expiratory flow
PIP	Pediatric Investigational Plan
PODCI	Pediatric Outcomes Data Collection Instrument
PSUR	Periodic Safety Update Report
PUL	Performance of the Upper Limb
PVC	premature ventricular contraction
QTc	corrected QT interval
QTcF	QTc corrected using Fridericia's formula
qual	qualitative
RBC	red blood cell
RRI	research-related injury
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	Standard deviation
SoA	schedule of activities
SRSD	Single Reference Safety Document
SUSAR	Suspected Unexpected Serious Adverse Reaction
T bili	total bilirubin
ULN	upper limit of normal
UL-PROM	Upper Limb Function Patient Reported Outcome Measure

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Abbreviation	Term
UL-PROM-CG	Upper Limb Function Patient Reported Outcome Measure Caregiver
US	United States
WBC	White blood cell

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