**Protocol C3391004**

# A NATURAL HISTORY STUDY IN CHINESE MALE PATIENTS WITH DUCHENNE MUSCULAR DYSTROPHY

## Statistical Analysis Plan (SAP)

**Version:** **2**

**Date:** 01 Jul 2022



[redacted]

## TABLE OF CONTENTS

## LIST OF TABLES

## APPENDICES

## 1. VERSION HISTORY

This Statistical Analysis Plan (SAP) for study C3391004 is based on the protocol amendment 2 dated 16 Jun 2022. This is the second version of the SAP (amendment 1).

**Table 1. Summary of Major Changes in SAP Amendments**

| Version/Date | Associated Protocol Amendment | Rationale | Specific Change |
|---|---|---|---|
| 1<br><br>20 Aug 2018 | Original<br><br>15 May 2018 | N/A | N/A |
| 2<br><br>01 Jul 2022 | Protocol Amendment 2<br>16 Jun 2022 | Issuance of a protocol amendment, template change | • Section 2.1: Added this section to align with the new SAP template.<br><br>• Section 2.2: Objectives and endpoints updated according to Protocol Amendment 2,<br><br>• Section 2.3: Updated study design according to Protocol Amendment 2.<br><br>• Section 3.1, 3.2: Primary and secondary endpoints updated according to the updated endpoints from Protocol Amendment 2.<br><br>• Section 3.4: Added detailed baseline variables.<br><br>• Section 4: Removed Section 4.1, 4.2, 4.3, 4.4, added table for analysis sets to align with the new SAP template.<br><br>• Section 5: Methodology updated according to the updated objectives and endpoints in Protocol Amendment 2; added Section 5.2.3 Analyses for Categorical Endpoints.<br><br>• Section 6: Added detailed analysis for Section 6.1, 6.2, 6.4, 6.5, 6.6; added |

**Table 1. Summary of Major Changes in SAP Amendments**

| Version/Date | Associated Protocol Amendment | Rationale | Specific Change |
|---|---|---|---|
| | | | Section 6.7 to address COVID-19 Pandemic Impacts.<br>• Section 7: Added the possible reviews of the data during the course of the study.<br>• Section 8: Added 2 references.<br>• Appendix 1.1: Added the definition and use of visit windows.<br>• Appendix 1.2: Added endpoint derivation rules for WPAI and PODCI.<br>• Appendix 2: Added List of Abbreviations. |

## 2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in study C3391004.

### 2.1. Modifications to the Analysis Plan Described in the Protocol

At present, there is no change in the analysis described in this SAP from those described in the protocol (Amendment 2).

### 2.2. Study Objectives, Endpoints, and Estimands

Estimands are not applicable in this study.

| Type | Objective: | Endpoints: |
|---|---|---|
| DMD disease characteristics | To characterize the natural history of Chinese DMD patients. | • Time to life-altering clinical milestones due to DMD disease progression, including:<br>  • Age at Failure to walk;<br>  • Age at Failure to stand;<br>  • Age at Failure to self-feed.<br>• Change from Baseline at each post-baseline visit in clinical evaluator (CE) determined scales: |

| Type | Objective: | Endpoints: |
|---|---|---|
| | | • Northstar Ambulatory Assessment (NSAA) total score (ambulatory children aged ≥3 years);<br>• Performance of Upper limb 2.0 (PUL 2.0) total score (subjects aged ≥10 years).<br>• Change from Baseline at each post-baseline visit in timed motor functions (Ambulatory subjects), including:<br>• Rise from floor velocity (supine to stand);*<br>• 10 meter walk/run velocity;*<br>• Change from Baseline at each post-baseline visit in strength of muscle groups (subjects aged ≥ 5 years):<br>• Knee extension;<br>• Elbow flexion;<br>• Elbow extension;<br>• Shoulder abduction.<br>• Change from Baseline at each post-baseline visit in range of motion (ROM) at bilateral ankles and elbows.<br>• Change from Baseline in pulmonary function tests (subjects aged ≥ 6 years) at Months 12, 24, and 30, including:<br>• Percent predicted Forced Vital Capacity (%pFVC);<br>• Percent predicted Forced Expiratory Volume in one Second (%pFEV$_1$);<br>• Maximum Inspiratory Pressure (MIP);<br>• Maximum Expiratory Pressure (MEP);<br>• Peak cough flow.<br>• Change from Baseline in cardiac functions at Months 12, 24, and 30, including:<br>• Left ventricular ejection fraction (LVEF).<br>• Change from Baseline in Wechsler Intelligence Scale for Children (WISC) score at Month 24 (ambulatory subjects aged ≥6 years to ≤16 years). |
| genetics | To characterize the prevalence of mutation types in Chinese DMD patients. | • DMD Mutation Type Endpoints:<br>• Proportion of subjects with mutation of exon deletion, exon duplication, point mutation, small insertion, small deletion, and others.<br>• The proportion of each affected exons by mutation types.<br>• The proportion of subjects with any mutation affecting any exon between exon 9 and exon 13, inclusive, or a deletion that affects both exon 29 and exon 30. |
| PRO | To characterize the quality of life in Chinese DMD patients. | • Quality of life endpoints:<br>• Change from Baseline in Pediatric Outcomes Data Collection Instrument (PODCI) Global Functioning Scale and each subscale scores at each post-baseline visit.<br>• Response to each of the 5 dimensions of EuroQoL 5 Dimension 3 Level (EQ-5D-3L)/ EuroQoL 5 Dimension Youth (EQ-5D-Y) and |

| Type | Objective: | Endpoints: |
|---|---|---|
| | | change from baseline in EQ-5D-3L/EQ-5D-Y（including VAS scores and index scores）at Months 12, 24, *and* 30. |
| health care utilization | To characterize the health care utilization in Chinese DMD patients. | • Health care utilization endpoints:<br>• Change from Baseline in Healthcare Resource Utilization (HRU) survey responses (including the number of office visits, out-of-pocket expenses, visits to the emergency room, and number of nights stayed in the hospital) at Months 12, 24, and 30.<br>• Change from Baseline in Work Productivity and Activity Impairment Questionnaire adapted for Caregiving (WPAI:CG) questionnaire scores (including absenteeism, presenteeism, work productivity loss, and activity impairment) at Months 12, 24, and 30. |

Note:
*The assessments rise from floor and walk/run 10 meters will be performed as part of NSAA assessment.

## 2.3. Study Design

This is a multicenter, prospective, single cohort study designed to describe the natural history of DMD in Chinese male patients. The study is planned to be conducted in 6-8 sites in China. A total of approximately 330 subjects will be enrolled with the target number of subjects in each group as below:

- Group 1, Ambulatory subjects aged <6 years, approximately 100 subjects;
- Group 2, Ambulatory subjects aged ≥6 years, approximately 180 subjects;
- Group 3, Non-ambulatory subjects, approximately 50 subjects.

Subjects will be enrolled in parallel for all age groups. Subjects who are too young to develop the ambulant ability will be considered ambulatory. Each subject will be observed for at least 24 months, i.e., the study will be ended 24 months after the last subject is enrolled such that all subjects have data through at least 24 months. All subjects will remain enrolled until the study completion date, such that some will have data collected after Month 24. Data collected during the first visit will be considered the Baseline assessments. The subjects will subsequently be assessed at Months 6, 12, 18, and 24. Subjects, who complete Visit 5/Month 24 at least 6 months prior to study completion, will be asked to complete an additional visit at Month 30. The end of study (EoS) Visit will be the last completed visit at Month 24 or 30. For any individual subject, the last study visit prior to study completion will be considered the end of study visit. During visit at Months 24, it will be determined whether the subjects will be able to attend the visit at Month 30, based on the projected study completion date.

No investigational drug is being studied or provided to subjects in this study. Subjects will be allowed to take medications prescribed by their physicians, which will constitute the standard of care (SOC). Subjects who are ≥4 years of age must be receiving GC for 6 months with at least 3 months on stable dose prior to study entry. Subjects who are aged <4 years will be exempt from this requirement; those not taking GC will be eligible if the initiation of GC treatment in these subjects is considered inappropriate in the opinion of Investigators. There is no restriction regarding other therapies for DMD or for concomitant conditions.

## 3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

### 3.1. Primary Endpoint(s)

#### 3.1.1. Time to Life Altering Clinical Milestones Due to DMD Disease Progression

- Age at failure to walk

  Age at failure to walk (in years) is defined as the age at the date of failure to walk. It will be calculated into one decimal (e.g., 7 years and 4 months will be 7.3 years) based on month and year of birth and month and year of failure to walk as reported by caregiver.

  Subjects who are not reported being failure to walk by their caregivers will be censored on the day of their last visit, and the age (in years) at censoring will be calculated as

  (date of last visit [in days] – date of birth [in days] + 1) / 365.25.

- Age at failure to stand

  Age at failure to stand (in years) is defined as the age at the date of failure to stand. It will be calculated into one decimal (e.g., 11 years and 4 months will be 11.3 years) based on month and year of birth and month and year of failure to stand as reported by caregiver.

  Subjects who are not reported being failure to stand by their caregivers will be censored on the day of their last visit, and the age (in years) at censoring will be calculated as

  (date of last visit [in days] – date of birth [in days] + 1) / 365.25.

- Age at failure to self-feed

  Age at failure to self-feed (in years) is defined as the age at the date of failure to self-feed. It will be calculated into one decimal (e.g., 16 years and 4 months will be 16.3 years) based on month and year of birth and month and year of failure to self-feed as reported by caregiver.

  Subjects who are not reported being failure to self-feed by their caregivers will be censored on the day of their last visit, and the age (in years) to censoring will be calculated as

(date of last visit [in days] – date of birth [in days] + 1) / 365.25.

### 3.1.2. Change from Baseline at Each Post-baseline Visit in Clinical Evaluator (CE) Determined Scales

- Change from baseline at each post-baseline visit in the North Star Ambulatory Assessment (NSAA) total score

  The NSAA is a 17-item test that grades performance of various functional skills using the following scale: 0 (unable to achieve goal independently), 1 (modified method but achieves goal with no physical assistance), and 2 ("normal"- no obvious modification of activity). 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.

  The NSAA will be performed in ambulatory children ≥3 years old.

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

- Change from baseline at each post-baseline visit in the Performance of Upper Limb (PUL) 2.0 total score

  The PUL 2.0 is a 22-item scale assessing high-level shoulder dimension (maximum score=12), mid-level elbow dimension (maximum score=17), and distal-level wrist and hand dimension (maximum score=13). The total score is calculated by adding the 3 level scores for a maximum global score of 42 with higher scores indicating better upper limb function. Based on the subject's score on an entry item, he will complete the entire scale or only the mid-level elbow and distal-level wrist and hand dimensions (the entry item score is not included in the total score).

  The PUL will be administered in subjects ≥10 years old.

  If the entry item score is ≤2, the individual items in the high-level shoulder dimension (items 1 to 6) will be set to a score of zero, and thus the high-level shoulder score =0. If one or more of the 22 individual items is/are missing, the total score is set to missing.

### 3.1.3. Change from Baseline at Each Post-baseline Visit in Timed Motor Functions (Ambulatory Subjects)

- Change from baseline at each post-baseline visit in the rise from floor velocity (ambulatory subjects)

  The rise from floor test will be assessed as part of NSAA. The rise from floor velocity is defined as the reciprocal of the time (in seconds) to rise from floor.

  The rise from floor test as part of NSAA will be performed in ambulatory children ≥3 years old.

For subjects with an NSAA Equivalent Activity score of 0 on the NSAA item of Rise from Floor, velocity will be set to 0. For subjects with a missing score on the NSAA item of Rise from Floor, velocity will be set to missing.

- Change from baseline at each post-baseline visit in the 10 meter walk/run velocity (ambulatory subjects)

  The 10 meter walk/run test will be performed as part of NSAA. The 10 meter walk/run velocity is defined as the reciprocal of the time (in seconds) to complete the 10 meter run/walk test.

  The 10 meter walk/run test as part of NSAA will be performed in ambulatory children ≥3 years old.

  For subjects with an NSAA Equivalent Activity score of 0 on the NSAA item of Run (10 meters), velocity will be set to 0. For subjects with a missing score on the NSAA item of Run (10 meters), velocity will be set to missing.

### 3.1.4. Change from Baseline at Each Post-baseline Visit in Strength of Muscle Groups

- Change from baseline at each post-baseline visit in knee extension
- Change from baseline at each post-baseline visit in elbow flexion
- Change from baseline at each post-baseline visit in elbow extension
- Change from baseline at each post-baseline visit in shoulder abduction

  The strength in muscle groups will be assessed by hand-held myometry as measured in kilogram (kg) for knee extension, elbow flexion, elbow extension, and shoulder abduction.

  Strength assessments will be done for both arms. Only data from the preferred arm will be included in the analysis. Information on the preferred arm will be collected on the PUL 2.0 CRF page.

  The assessment will be performed in subjects ≥5 years old.

### 3.1.5. Change from Baseline at Each Post-baseline Visit in Range of Motion (ROM) at Bilateral Ankles and Elbows

- Change from baseline at each post-baseline visit in ROM at bilateral ankles

  The ROM at left and right ankles will be measured in degrees of passive dorsiflexion. The range of dorsiflexion past plantargrade is documented as positive degrees of dorsiflexion, while the range lacking from plantargrade is documented as negative degrees of dorsiflexion.

- Change from baseline at each post-baseline visit in ROM at bilateral elbows

  The ROM at left and right elbows will be measured in degrees of passive extension. The range of elbow extension lacking from neutral is documented as negative degrees of extension.

### 3.1.6. Change from Baseline in Pulmonary Function Tests (PFTs) at Months 12, 24, and 30.

- Change from baseline at Months 12, 24, and 30 in percent predicted Forced Vital Capacity (%pFVC)

  The %pFVC is measured in percentage (%) and will be calculated from FVC (measured in liter [L]) according to age, height (estimated height as derived from the ulna length for non-ambulatory subjects), ethnicity, and gender using multi-ethnic reference values for spirometry for the 3 to 95 year age range as published by the Global Lung Function Initiative Network[1].

- Change from baseline at Months 12, 24, and 30 in percent predicted Forced Expiratory Volume in one Second (%pFEV$_1$)

  The %pFEV$_1$ is measured in percentage (%) and will be calculated from FEV$_1$ (measured in liter [L]) according to age, height (estimated height as derived from the ulna length for non-ambulatory subjects), ethnicity, and gender using multi-ethnic reference values for spirometry for the 3 to 95 year age range as published by the Global Lung Function Initiative Network[1].

- Change from baseline at Months 12, 24, and 30 in Maximum Inspiratory Pressure (MIP)

  The MIP is measured in cm H2O.

- Change from baseline at Months 12, 24, and 30 in Maximum Expiratory Pressure (MEP)

  The MEP is measured in cm H2O.

- Change from baseline at Months 12, 24, and 30 in Peak Cough Flow (PCF)

  PCF is measured in liter per minute (L/min).

The pulmonary function assessments will be performed in subjects ≥6 years old.

### 3.1.7. Change from Baseline in Cardiac Functions at Months 12, 24, and 30.

- Change from baseline at Months 12, 24, and 30 in left ventricular ejection fraction (LVEF)

  The LVEF is measured in percentage (%).

### 3.1.8. Change from Baseline in Wechsler Intelligence Scale for Children (WISC) Score at Month 24.

- Change from baseline in Wechsler Intelligence Scale for Children (WISC) score at Month 24

  The WISC-IV is individually administered intelligence test for children between ages of 6 and 16. It generates a Full Scale Intelligence Quotient (IQ) (formerly known as an intelligence quotient or IQ score) that represents a child's general intellectual ability. It also provides four primary index scores: Verbal Comprehension Index, Perceptual Reasoning Index, Working Memory Index, and Processing Speed Index. These indices represent a child's abilities in discrete cognitive domains. The WISC will be performed in ambulatory subjects aged ≥6 years to ≤16 years.

## 3.2. Secondary Endpoint(s)

### 3.2.1. DMD Mutation Type Endpoints

- Proportion of subjects with mutation of exon deletion, exon duplication, point mutation, small insertion, small deletion, and others.
- The proportion of each affected exons by mutation types.
- The proportion of subjects with any mutation affecting any exon between exon 9 and exon 13, inclusive, or a deletion that affects both exon 29 and exon 30.

### 3.2.2. Quality of Life (QoL) Endpoints

#### 3.2.2.1. PODCI

- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale and each subscale scores (pediatric parent).
- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale and each subscale scores (adolescent parent).
- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale and each subscale scores (adolescent self report).

The PODCI is a patient-reported assessment of musculoskeletal health intended for use in children and adolescents. The pediatric version is intended for completion by parents or caregivers of children ≤10 years old. The adolescent versions will be completed by subjects 11-18 years old and also by their parents or caregivers. The instrument is organized into multiple domains: upper extremity and physical function, transfer and basic mobility, sports and physical functioning, pain/comfort, happiness. Each domain produces an independent score, and a total score is also computed. Scores will be reported as standardized.

The PODCI Global Functioning Scale is derived from the means of first four core scales. Higher scores represent better physical function and psychological well-being. The

derivation of each core scales and the Global Functioning Scale including the rule for handling missing items is provided in Appendix 1.2.2.

#### 3.2.2.2. EQ-5D-3L

- EQ-5D-3L assessment at Months 12, 24, and 30.
  - Response to each of the 5 dimensions of the EQ-5D-3L assessment;
  - Change from baseline in the EQ-5D-3L index score;
  - Change from baseline in the EQ-5D-3L VAS assessment.

The EQ-5D-3L is a questionnaire completed by the subject, designed to assess the subject's current health and translate that score into an index value or utility score, providing a mechanism for conducting cost-effectiveness and cost-utility analyses. There are two components to the EQ-5D-3L: a Health State Profile and a visual analog scale (VAS) item. The Health State Profile is described in terms of 5 dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. The responses record three levels of severity (no problems/some or moderate problems/extreme problems) within a particular ED-5D dimension and are calculated to form a single index value.

EQ-5D-3L will be completed by subjects who are aged ≥16 years.

#### 3.2.2.3. EQ-5D-Y

- EQ-5D-Y assessment at Months 12, 24, and 30.
  - Response to each of the 5 dimensions of the EQ-5D-Y assessment;
  - Change from baseline in the EQ-5D-Y VAS assessment.

The EQ-5D-Y is a newly developed generic instrument measuring health-related quality of life in children and adolescents younger than 16 years old. It was adapted from the EQ-5D original questionnaire.

EQ-5D-Y will be completed by subjects who are aged <16 years and able to read and complete the questionnaire.

### 3.2.3. Health Care Utilization Endpoints

#### 3.2.3.1. HRU survey

- Change from baseline at Months 12, 24, and 30 in the HRU survey:
  - Number of office visits;
  - Out-of-pocket expenses;
  - Visits to the emergency room;

- Number of nights stayed in the hospital.

The HRU questionnaire is completed by the caregiver and asks questions about healthcare resources utilization related to their child's use of healthcare professionals, emergency room visits, and hospitalizations during the course of the study. Caregivers are also asked to estimate out-of-pocket costs related to healthcare resource utilization.

#### 3.2.3.2. WPAI

- Change from baseline at Months 12, 24, and 30 in WPAI:CG scores:
  - Absenteeism;
  - Presenteeism;
  - Work productivity loss; and
  - Activity impairment.

  The WPAI:CG is a self-reported measure of work productivity and impairment, to be completed by the caregiver, that yields four scores: Absenteeism (work time missed); Presenteeism (impairment at work/reduced on the job effectiveness); work productivity loss (overall work impairment/absenteeism plus presenteeism); and activity impairment. Each score is expressed as a percentage (0-100%) with higher numbers indicating greater impairment and less productivity. The derivation of each score including the rule for handling missing items is provided in Appendix 1.2.1.

### 3.3. Other Endpoint(s)

None.

### 3.4. Baseline Variables

The baseline is collected on Day 1 (Visit 1).

- Demographic characteristics including age, race, ethnicity, racial designation and residence area (urban/rural) where age is calculated following Pfizer data standards as age in years at the baseline visit.
- Physical measurements at the baseline visit include height (cm), ulna length (cm), estimated height (cm) if ulna length is nonmissing and weight (kg). The estimated height will be calculated follow the method developed by Gauld[2].
- Family history of disease.
- Glucocorticoid regimen (including specific medication and daily dose in mg/kg, and duration of current glucocorticoid regimen use) at the baseline visit, and age at initiation of any glucocorticoid use (years/months).

- General medical history, including diseases or syndromes that are ongoing ('present') at, or stopped ('past') before baseline visit. The Medical Dictionary for Regulatory Activities (MedDRA) will be used to code the disease/syndrome.

- Medications taken prior to baseline visit.

### 3.5. Safety Endpoints

Standard safety data such as vital signs, physical exams, laboratory data, adverse events, etc. will also be collected during the study according to Pfizer data standard.

## 4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

| Population | Description | Applicable Analysis (for additional information refer to section 6) |
|---|---|---|
| Entered | All participants who sign the informed consent document. | Participant Evaluation |
| Full Analysis Set (FAS) | All subjects who have been enrolled in the study and have at least one of the primary endpoint data collected after baseline. | Analysis for primary and secondary endpoints, baseline summary, disposition. |
| Safety Analysis Set (SAS) | All subjects who have been enrolled in the study. | Safety analysis |

## 5. GENERAL METHODOLOGY AND CONVENTIONS

### 5.1. Hypotheses and Decision Rules

Not applicable.

### 5.2. General Methods

In general, all summaries for primary and secondary endpoints, baseline summaries, participant disposition, and concomitant medications will be performed within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined where applicable.

#### 5.2.1. Analyses for Binary Endpoints

Binary endpoints will be descriptively summarized. Sample size, count and percentage will be reported.

#### 5.2.2. Analyses for Continuous Endpoints

Continuous endpoints will be descriptively summarized. Sample size, mean, standard deviation, median, minimum and maximum will be reported.

### 5.2.3. Analyses for Categorical Endpoints

Categorical endpoints will be descriptively summarized. Sample size, count and percentage for each level will be reported.

### 5.2.4. Analyses for Time-to-Event Endpoints

Kaplan-Meier (product limit) method will be used for estimation of proportion of participants with event, time-to-event curve, median (95% CI) time-to-event.

## 5.3. Methods to Manage Missing Data

Missing data will not be imputed in this study.

# 6. ANALYSES AND SUMMARIES

## 6.1. Primary Endpoints

### 6.1.1. Time to Life-Altering Clinical Milestones Due to DMD Disease Progression

Endpoints:

- Age at failure to walk
- Age at failure to stand
- Age at failure to self-feed

Analysis:

- Analysis set: FAS.
- Analysis methodology: Ages in years will be summarized within each of the Group 1, 2, 3 and 3 groups combined using the K-M method (Section 5.2.4).
- Missing data: All available data including censoring information for subjects will be included. Missing data will not be imputed.
- Within each of the Group 1, 2, 3 and 3 groups combined,
    - Summary statistics (N, n, mean, SD, median, Q1, Q3, minimum, and maximum) will be presented for the age of the subject at which event occurs.
    - Median, Q1, Q3 of age at which event occurs will be provided with 95% CIs, and number (%) of censored subjects will also be reported.

Graphical display:

- The estimated K-M curves for 3 groups combined will be displayed graphically.

### 6.1.2. Change from Baseline at Each Post-baseline Visit in CE Determined Scales

Endpoints:

- Change from baseline at each post-baseline visit in NSAA total score
- Change from baseline at each post-baseline visit in PUL 2.0 scores, including,
    - PUL 2.0 total score;
    - PUL high-level shoulder;
    - PUL mid-level elbow;
    - PUL distal-level wrist and hand

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where NSAA is assessed for observed values and changes from baseline will be provided within each of the Group 1, 2 and for 2 groups combined (ambulatory subjects).
- Same descriptive summary of PUL 2.0 scores will be provided for Group 2 (ambulatory subjects), Group 3 (non-ambulatory subjects), and for 2 groups combined.

Graphical display:

- Mean (SD) of observed NSAA total scores for each age at baseline will be displayed graphically by visits for Group 1, 2 combined (ambulatory subjects).
- Mean (SD) of changes from baseline in NSAA total score for each age at baseline will be displayed graphically by visits for Group 1, 2 combined (ambulatory subjects).
- Mean (SD) of observed PUL 2.0 total scores for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.
- Mean (SD) of changes from baseline in PUL 2.0 total score for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

### 6.1.3. Change from Baseline at Each Post-baseline Visit in Timed Motor Functions (Ambulatory Subjects)

Endpoints:

- Change from baseline at each post-baseline visit in rise from floor velocity (ambulatory subjects)
- Change from baseline at each post-baseline visit in 10 meter walk/run velocity (ambulatory subjects)

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where NSAA is assessed for observed values and changes from baseline will be provided within each of the Group 1, 2, and for 2 groups combined (ambulatory subjects).

Graphical display:

- Mean (SD) of observed values for each age at baseline will be displayed graphically by visits for Group 1,2 combined (ambulatory subjects).
- Mean (SD) of changes from baseline for each age at baseline will be displayed graphically by visits for Group 1, 2 combined (ambulatory subjects).

### 6.1.4. Change from Baseline at Each Post-baseline Visit in Strength of Muscle Groups

Endpoints:

- Change from baseline at each post-baseline visit in knee extension
- Change from baseline at each post-baseline visit in elbow flexion
- Change from baseline at each post-baseline visit in elbow extension
- Change from baseline at each post-baseline visit in shoulder abduction

Analysis:

- Analysis set: FAS.

- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where strength of muscle groups is assessed for observed values and changes from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

Graphical display:

- Mean (SD) of observed values for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.
- Mean (SD) of changes from baseline for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

### 6.1.5. Change from Baseline at Each Post-baseline Visit in ROM at Bilateral Ankles and Elbows

Endpoints:

- Change from baseline at each post-baseline visit in ROM at bilateral ankles
- Change from baseline at each post-baseline visit in ROM at bilateral elbows

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- For each side, N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where ROM is assessed for observed values and changes from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

Graphical display:

- For each side, mean (SD) of observed values for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

- For each side, mean (SD) of changes from baseline for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

### 6.1.6. Change from Baseline in PFTs at Months 12, 24, and 30

Endpoints:

- Change from baseline at Months 12, 24, and 30 in %pFVC (including FVC)
- Change from baseline at Months 12, 24, and 30 in %p$FEV_1$ (including $FEV_1$)
- Change from baseline at Months 12, 24, and 30 in MIP
- Change from baseline at Months 12, 24, and 30 in MEP
- Change from baseline at Months 12, 24, and 30 in PCF

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and Months 12, 24, and 30 where pulmonary function test is assessed for observed values and changes from baseline will be provided for Group 2 (ambulatory subjects), Group 3 (non-ambulatory subjects), and for 2 groups combined.

Graphical display:

- Mean (SD) of observed values for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.
- Mean (SD) of changes from baseline for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

### 6.1.7. Change from Baseline in Cardiac Functions at Months 12, 24, and 30

Endpoint: Change from baseline at Months 12, 24, and 30 in LVEF

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.

- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 12, 24 and 30) where cardiac function is assessed for observed values and changes from baseline will be provided for Group 2 (ambulatory subjects), Group 3 (non-ambulatory subjects), and for 2 groups combined.

Graphical display:

- Mean (SD) of observed values for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.
- Mean (SD) of changes from baseline for each age at baseline by ambulatory status (ambulatory versus non-ambulatory) will be displayed graphically by visits.

#### 6.1.8. Change from Baseline in WISC Score at Month 24

Endpoint: Change from baseline at Month 24 in WISC score

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and Months 24 where WISC is assessed for observed values and changes from baseline will be provided for Group 2 (ambulatory subjects).

Graphical display:

- Mean (SD) of observed values at baseline and Month 24 will be displayed graphically by age at baseline for Group 2 (ambulatory subjects).
- Mean (SD) of changes from baseline at Month 24 will be displayed graphically by age at baseline for Group 2 (ambulatory subjects).

### 6.2. Secondary Endpoint(s)

#### 6.2.1. DMD Mutation Type Endpoint

Dystrophin mutation type will be summarized within each of the Group 1, 2, 3 and for 3 groups combined using number (%) of participants.

Endpoints:

- Proportion of subjects with mutation of exon deletion, exon duplication, point mutation, small insertion, small deletion, and others.
- The proportion of each affected exons by mutation types.
- The proportion of subjects with any mutation affecting any exon between exon 9 and exon 13, inclusive, or a deletion that affects both exon 29 and exon 30.

Analysis

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, count and percentage will be reported within each of the Group 1, 2, 3, and for 3 groups combined.

Graphical display:

- The frequency (count) and proportion (count/n*100%) of each affected exon by mutation types will be plotted for 3 groups combined.

### 6.2.2. QoL Endpoint

#### 6.2.2.1. PODCI

Endpoints:

- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale (pediatric parent).
- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale (adolescent parent).
- Change from baseline at each post-baseline visit in the PODCI Global Functioning Scale (adolescent self report).

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.

- For global functioning scale and each of core scales (upper extremity and physical function, transfer and basic mobility, sports and physical functioning, pain/comfort, happiness), N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1) and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where PODCI is assessed for observed values and changes from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

#### 6.2.2.2. EQ-5D-3L

Endpoint: Response to each of the 5 dimensions of the EQ-5D-3L assessment at Months 12, 24, and 30

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- For each of the 5 dimensions, the number and percentage of participants responding as 'no problems', 'some problems', or 'extreme problems' at baseline, Months 12, 24, and 30 will be provided for Group 2 (ambulatory subjects), Group 3 (non-ambulatory subjects), and for 2 groups combined.

Endpoints:

- Change from baseline in the EQ-5D-3L index score at Months 12, 24, and 30;
- Change from baseline in the EQ-5D-3L VAS assessment at Months 12, 24, and 30.

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1), Months 12, 24, and 30 for observed values and changes from baseline will be provided for Group 2 (ambulatory subjects), Group 3 (non-ambulatory subjects), and for 2 groups combined.

#### 6.2.2.3. EQ-5D-Y

Endpoint: Response to each of the 5 dimensions of the EQ-5D-Y assessment at Months 12, 24, and 30

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- For each of the 5 dimensions, the number and percentage of participants responding as 'no problems', 'some problems', or 'extreme problems' at baseline, Months 12, 24, and 30 will be provided within each of the group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

Endpoint: Change from baseline in the EQ-5D-Y VAS assessment at Months 12, 24, and 30.

Analysis:

- Analysis set: FAS.
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline (Day 1), Months 12, 24, and 30 for observed values and changes from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

### 6.2.3. Health Care Utilization Endpoints

#### 6.2.3.1. HRU survey

Endpoint: Change from baseline at each post-baseline visit in the HRU survey, including:

- Number of office visits;
- Out-of-pocket expenses;
- Visits to the emergency room; and
- Number of nights stayed in the hospital.

Analysis:

- Analysis set: FAS
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- If a participant changes his caregiver during the reporting period, from the one at baseline, all values collected after the change will be set to missing.
- For number of office visits, N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where HRU survey is assessed for the observed value and change from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined for:
  - Total number of office visits;
  - Number of office visits for primary care physician, general practitioner, and physician assistant or nurse practitioner;
  - Number of office visits for specialist;
  - Number of office visits for psychologist and other therapist;
  - Number of office visits for physical therapist and occupational therapist;
  - Number of office visits for other.
- For out-of-pocket expenses, N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and all post-baseline visits (i.e., Months 6, 12, 18, 24, and 30) where HRU survey is assessed for the observed value and change from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined in Chinese Yuan.
- For number of visits to the emergency room and number of nights stayed in the hospital, the number and percent of participants with 0, 1, 2, 3, etc. visits/nights at baseline and all post-baseline visits where HRU survey is assessed will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined; and N, n, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and all post-baseline visits where HRU survey is assessed for the observed value and change from baseline in number of visits/nights will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined.

#### 6.2.3.2. WPAI

Endpoint: Change from baseline at each post-baseline visit in WPAI impairment scores, including:

- Absenteeism: percent work time missed;
- Presenteeism: percent impairment while working;
- Work productivity loss: percent overall work impairment;
- Activity impairment: percent activity impairment.

Analysis

- Analysis set: Caregivers of participants in FAS
- Analysis methodology: Not applicable.
- Missing data: All available data will be included. Missing data will not be imputed.
- For each participant's caregiver at baseline, N, mean, SD, median, Q1, Q3, minimum, and maximum at baseline and all post-baseline visits where the WPAI questionnaire is assessed for the observed value and change from baseline will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined. If a participant changes his caregiver during the reporting period, from the one at baseline, all values collected after the change will be set to missing.

### 6.3. Other Endpoint

None.

### 6.4. Subset Analyses

In general, all analysis for primary and secondary endpoints, baseline summaries, participant disposition, and concomitant medications will be applied within each of the Group 1, 2, 3, and by ambulatory status (ambulatory versus non-ambulatory) where applicable.

### 6.5. Baseline and Other Summaries and Analyses

#### 6.5.1. Baseline Summaries

1. Demographic characteristics will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined

according to Pfizer data standards. Number of subjects in the screening age categories below will be displayed graphically for,

- Group 1 and 2: age in 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, and ≥15 years;
- Group 3: age in ≤7, 8, 9, 10, 11, 12, 13, 14, 15, 16, and ≥17 years.

2. Baseline physical measurements (including height, ulna length, estimated height and weight) will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards.

3. Background glucocorticoid regimen will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined. Prednisolone and prednisone will be combined for this analysis. The number (%) of subjects for each glucocorticoid being received at baseline visit will be presented. Descriptive statistics (N, mean, SD, median, minimum, and maximum) will be presented for

   - Daily dose (mg/kg) for each glucocorticoid the subject is receiving at baseline. This will be calculated from the total daily dose and baseline weight collected in the CRF.
   - Duration of glucocorticoid use (months) for glucocorticoid dose the subject is receiving at baseline.

4. Significant medical history will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards.

5. Prior medications will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards.

### 6.5.2. Study Conduct and Participant Disposition

1. The below populations/sets will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards,

   - FAS
   - SAS

2. Patients disposition (e.g., discontinuation from study, reason for discontinuation, completed study, and ongoing) based on FAS will be summarized within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards.

### 6.5.3. Concomitant Medications and Nondrug Treatments

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

The number (%) of subjects who took each concomitant medication will be provided within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined according to Pfizer data standards.

## 6.6. Safety Summaries and Analyses

All safety analysis will be performed on the SAS.

### 6.6.1. Adverse Events

AEs for research related injury will be listed. All AEs will be listed.

### 6.6.2. Laboratory Data

Incidence of laboratory test abnormalities during the reporting period will be summarized within each of the Group 1, 2, 3, without regard to baseline abnormality, for normal baseline, and for abnormal baseline according to Pfizer data standards. Any adverse events related to laboratory test abnormalities will be included in the adverse event analysis.

Changes and percent changes from baseline in creatine kinase (CK) will be summarized descriptively in tabular format by visit within each of the Group 1, 2, 3, by ambulatory status (ambulatory versus non-ambulatory), and for 3 groups combined. Changes from baseline in CK will be displayed graphically by visit for each age at baseline by ambulatory status (ambulatory versus non-ambulatory).

### 6.6.3. Vital Signs

No specific data summaries will be provided for vital signs. Any adverse events related to vital signs will be included in the adverse event analysis.

### 6.6.4. Electrocardiograms (ECG)

No specific data summaries will be provided for ECG. Any adverse events related to ECG will be included in the adverse event analysis.

### 6.6.5. Physical Examination

No specific data summaries will be provided for physical examinations. Any adverse events related to Physical Examination will be included in the adverse event analysis.

## 6.7. Additional Analyses to Address COVID-19 Pandemic Impacts

- Protocol deviations related to COVID-19 pandemic will be summarized and listed separately. Both important and non-important PDs related to COVID-19 pandemic will be reported.

- A separate summary table solely for subject discontinuations related to COVID-19 pandemic, if any, will be provided.
- COVID-19 related AEs, if any, will be reported.

## 7. INTERIM ANALYSES

### 7.1. Introduction

No formal interim analyses will be conducted for this study. The sponsor may conduct reviews of the data during the course of the study to support clinical development.

### 7.2. Interim Analyses and Summaries

Not applicable.

## 8. REFERENCES

1. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012;40(6):1324-43.

2. Gauld LM, Kappers J, Carlin JB, Robertson CF. Height prediction from ulna length. Dev Med Child Neurol. 2004;46(7):475-80.

# APPENDICE

## Appendix 1. Data Derivation Details

### Appendix 1.1. Definition and Use of Visit Windows in Reporting

Visit windows will be developed for specific data points in reference to SoA, so the data may be summarized by visit window. If multiple nonmissing values are observed within a window, the value closest (and prior) to the target day will be included in the analysis. The most abnormal value of the categorical measurements will be used for categorization.

### Appendix 1.2. Endpoint Derivations

#### Appendix 1.2.1. WPAI scoring

WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes, as follows:

Questions:

Q1 = currently employed

Q2 = hours missed due to health problems

Q3 = hours missed other reasons

Q4 = hours actually worked

Q5 = degree health affected productivity while working

Q6 = degree health affected regular activities

Scores:

Multiply scores by 100 to express in percentages.

Percent work time missed due to health: Q2/(Q2+Q4)

Percent impairment while working due to health: Q5/10

Percent overall work impairment due to health: Q2/(Q2+Q4)+[(1-(Q2/(Q2+Q4)))x(Q5/10)]

Percent activity impairment due to health: Q6/10

#### Appendix 1.2.2. PODCI

Missing Items: If an item contained within a scale is not answered, that item is not computed into the mean used for that scale.

Standardized scores should be rounded to the nearest whole number. Standardized scores are calculated so that a "0" represents a poor outcome/worse health while "100" is the best possible outcome/best health.

The Pediatric (Parent Report), Adolescent (Self Report), and Adolescent (Parent Report) versions of the PODCI include a Global Function Scale in addition to the following core scales:

1. Upper Extremity and Physical Function Core Scale (8 items)
   a. Q1, Q2, Q3, Q4, Q5, Q6, Q8, Q32
2. Transfer and Basic Mobility Core Scale (11 items)
   a. Q7, Q21, Q24, Q25, Q28, Q29, Q30, Q31, Q33, Q34, Q35
3. Sports and Physical Functioning Core Scale (21 items)
   a. Pediatric and Adolescent (Parent report): Q18, Q19, Q20, Q22, Q23, Q26, Q27, Q36 (conditional on Q42 too young and Q43 activity not in season), Q44 (conditional on Q50 too young and Q51 activity not in season), Q52 (conditional on Q58 too young and Q59 activity not in season), Q60 (conditional on Q65 friends not around), Q66 (conditional on Q72 school not in session and Q73 does not attend school)
   b. Adolescent (Self Report): Q18, Q19, Q20, Q22, Q23, Q26, Q27, Q36 (conditional on Q42 activity not in season), Q43 (conditional on Q49 activity not in season), Q50 (conditional on Q56 activity not in season), Q57 (conditional on Q62 friends not around), Q63 (conditional on Q69 school not in session and Q70 does not attend school)
4. Pain/Comfort Core Scale (3 items)
   a. Pediatric and Adolescent (Parent report): Q17, Q75, Q76
   b. Adolescent (Self Report): Q17, Q72, Q73
5. Happiness Core Scale (5 items)
   a. Q10, Q11, Q12, Q13, Q14

**1. Pediatric (Parent Report) and Adolescent (Parent Report) scoring**

**a. The algorithm for the upper extremity and physical function core scale is as follows:**

i. Notes:
   1) Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.
   2) A minimum of 4 items must have valid answers to score this scale (including those marked "too young" as missing).

ii. Mean of Items = (sum of items Q1, Q2, Q3, Q4, Q5, Q6, Q8, Q32)/ (number of non-missing items)

**iii.** Standardized Score = [(4 - mean of items)/3]*100

**b. The algorithm for the transfer and basic mobility core scale is as follows:**

i. Notes:
   1) Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.
   2) A minimum of 7 items must have valid answers to score this scale (including those marked "too young" as missing).
   3) Q34rescaled = [(Q34-1)*3/4]+1, Q35rescaled = [(Q35-1)*3/4]+1.

ii. Mean of Items = (sum of items Q7, Q21, Q24, Q25, Q28, Q29, Q30, Q31, Q33, Q34Rescaled, Q35Rescaled) / (number of non-missing items)

iii. Standardized Score = [(4 - mean of items)/3]*100

**c. The algorithm for the sports and physical functioning core scale is as follows:**

i. Notes:
   1) Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.
   2) A minimum of 6 items must have valid answers to score this scale (including those marked "too young" as missing).
   3) Q26rescaled = [ (Q26 -1) * 3/4] + 1, Q27rescaled = [ (Q27 -1) * 3/4] + 1.
   4) Q36 is RECODED to MISSING if (Q36 = 4 and EITHER [Q42 = 1] or [Q43 = 1])
   5) Q44 is RECODED to MISSING if (Q44 = 4 and EITHER [Q50 = 1] or [Q51 = 1])
   6) Q52 is RECODED to MISSING if (Q52 = 4 and EITHER [Q58 = 1] or [Q59 = 1])
   7) Q60 is RECODED and RESCALED as follows:
      - Step #1: Q60 is RECODED to MISSING if (Q60 = 3 and Q65 = 1)
      - Step #2: If Q60 is not missing, Q60rescaled = [(Q60-1)*3/2]+1
   8) Q66 is RECODED and RESCALED as follows:
      - Step #1: Q66 is RECODED to MISSING if (Q66 = 4)
      - Step #2: Q66 is RECODED to MISSING if (Q66 = 3 and EITHER [Q72 = 1] or [Q73 = 1])
      - Step #3: If Q66 is not missing, Q66rescaled = [(Q66-1)*3/2]+1

ii. Mean of Items = (sum of items Q18, Q19, Q20, Q22, Q23, Q26rescaled, Q27rescaled, Q36, Q44, Q52, Q60rescaled, Q66rescaled) / (number of non-missing items)

iii. Standardized Score = [(4 - mean of items) /3]*100

**d. The algorithm for the pain/comfort core scale is as follows:**

i. Notes:
   1) A minimum of 2 items must have valid answers to score this scale.
   2) Q17rescaled = [(4-Q17)*4/3]+1, Q75rescaled = [(Q75-1)*4/5]+1.
ii. Mean of Items = (sum of items Q17rescaled, Q75rescaled, Q76) / (number of non-missing items)
iii. Standardized Score = [(4-{mean of items - 1})/4]*100

**e. The algorithm for the happiness core scale is as follows:**

i. Notes:
   1) Any item rated "5" (Too young for this activity) is considered missing and is not added into the scale.
   2) A minimum of 3 items must have valid answers to score this scale (including those marked "too young" as missing).
ii. Mean of Items = (sum of items Q10, Q11, Q12, Q13, Q14) / (number of non-missing items)
iii. Standardized Score = [(5 - mean of items)/ 4]*100

**f. The algorithm for the Global Function scale is as follows:**

i. Notes: If ANY of the four relevant scales are missing, this is not calculated.
ii. Standardized Score = (sum of standardized scores for scales: 'Upper extremity and physical function' + 'Transfer and basic mobility' + Sports and physical function' and 'Pain/comfort') /4

**2. Adolescent (Self Report) scoring**

**a. The algorithm for the upper extremity and physical function core scale is as follows:**

i. Notes:
   1) A minimum of 4 items must have valid answers to score this scale.
ii. Mean of Items = (sum of items Q1, Q2, Q3, Q4, Q5, Q6, Q8, Q32)/ (number of non-missing items)
iii. Standardized Score = [(4 - mean of items)/3]*100

**b. The algorithm for the transfer and basic mobility core scale is as follows:**

i. Notes:
   1) A minimum of 7 items must have valid answers to score this scale.
   2) Q34rescaled = [(Q34-1)*3/4]+1, Q35rescaled = [(Q35-1)*3/4]+1.

ii. Mean of Items = (sum of items Q7, Q21, Q24, Q25, Q28, Q29, Q30, Q31, Q33, Q34Rescaled, Q35Rescaled) / (number of non-missing items)
iii. Standardized Score = [(4 - mean of items)/3]*100

**c. The algorithm for the sports and physical functioning core scale is as follows:**

i. Notes:
   1) A minimum of 6 items must have valid answers to score this scale.
   2) Q26rescaled = [(Q26-1)*3/4]+1, Q27rescaled = [(Q27-1)*3/4]+1.
   3) Q36 is RECODED to MISSING if (Q36 = 4 and Q42 = 1)
   4) Q43 is RECODED to MISSING if (Q43 = 4 and Q49 = 1)
   5) Q50 is RECODED to MISSING if (Q50 = 4 and Q59 = 1)
   6) Q57 is RECODED and RESCALED as follows:
      - Step #1: Q57 is RECODED to MISSING if (Q57 = 3 and Q62 = 1)
      - Step #2: If Q57 is not missing, Q57rescaled = [(Q57-1)* 3/2]+1
   7) Q63 is RECODED and RESCALED as follows:
      - Step #1: Q63 is RECODED to MISSING if (Q63 = 4)
      - Step #2: Q63 is RECODED to MISSING if (Q63 = 3 and EITHER [Q69 = 1] or [Q70 = 1] )
      - Step #3: If Q63 is not missing, Q63rescaled = [(Q63-1)*3/2]+1

ii. Mean of Items = (sum of items Q18, Q19, Q20, Q22, Q23, Q26rescaled, Q27rescaled, Q36, Q43, Q50, Q57rescaled, Q63rescaled) / (number of non-missing items)
iii. Standardized Score = [(4 - mean of items)/3]*100

**d. The algorithm for the pain/comfort core scale is as follows:**

i. Notes:
   1) A minimum of 2 items must have valid answers to score this scale.
   2) Q17rescaled = [(4-Q17)*4/3]+1, Q72rescaled = [(Q72-1)*4/5]+1.
ii. Mean of Items = (sum of items Q17rescaled, Q72rescaled, Q73) / (number of non-missing items)
iii. Standardized Score = [(4-{mean of items - 1})/ 4]*100

**e. The algorithm for the happiness core scale is as follows:**

i. Notes:
   1) A minimum of 3 items must have valid answers to score this scale.

ii. Mean of Items = (sum of items Q10, Q11, Q12, Q13, Q14) / (number of non-missing items)
iii. Standardized Score = [(5 - mean of items)/ 4]*100

**f. The algorithm for the Global Function scale is as follows:**

i. Notes: If ANY of the four relevant scales are missing, this is not calculated.
ii. Standardized Score = (sum of standardized scores for scales: 'Upper extremity and physical function' + 'Transfer and basic mobility' + Sports and physical function' and 'Pain/comfort') /4

## Appendix 2. List of Abbreviations

| Abbreviation | Term |
|---|---|
| AE | adverse event |
| CE | Clinical Evaluator |
| CI | confidence interval |
| CK | creatine kinase |
| cm | centimeter |
| COVID | coronavirus disease |
| CRF | case report form |
| DMD | Duchenne muscular dystrophy |
| ECG | electrocardiogram |
| EoS | end of study |
| EQ 5D Y | EuroQoL 5 Dimension Youth |
| EQ 5D 3L | EuroQoL 5 Dimension 3 Level |
| FAS | full analysis set |
| $FEV_1$ | Forced Expiratory Volume in one Second |
| $\%pFEV_1$ | percent predicted Forced Expiratory Volume in one Second |
| FVC | Forced Vital Capacity |
| %pFVC | percent predicted Forced Vital Capacity |
| GC | glucocorticosteroids |
| HRU | Healthcare Resource Utilization |
| IQ | Intelligence Quotient |
| kg | kilogram |
| K-M | Kaplan-Meier |
| L | liter |
| LVEF | left ventricular ejection fraction |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MEP | Maximum Expiratory Pressure |
| MIP | Maximum Inspiratory Pressure |
| min | minute |
| N/A | not applicable |
| NSAA | North Star Ambulatory Assessment |
| PCF | Peak Cough Flow |
| PD | protocol deviation |
| PFT | Pulmonary Function Test |
| PODCI | Pediatric Outcomes Data Collection Instrument |
| PRO | patient-reported outcome |
| PUL | Performance of Upper Limb |
| QoL | Quality of Life |
| Q1 | first quartile |
| Q3 | third quartile |
| ROM | Range of Motion |
| SAE | serious adverse event |

| Abbreviation | Term |
|---|---|
| SAP | statistical analysis plan |
| SAS | Safety Analysis Set |
| SD | standard deviation |
| SoA | Schedule of activities |
| SOC | standard of care |
| VAS | visual analog scale |
| WHO | World Health Organization |
| WISC | Wechsler Intelligence Scale for Children |
| WPAI:CG | Work Productivity and Activity Impairment Questionnaire adapted for Caregiving |