STATISTICAL ANALYSIS PLAN

AN OPEN-LABEL, SAFETY STUDY FOR ATALUREN (PTC124) PATIENTS WITH NONSENSE MUTATION DYSTROPHINOPATHY

PTC124-GD-016-DMD

21 NOVEMBER 2025

VERSION 1.0

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APPROVAL SIGNATURES

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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

Abbreviation	Term
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
DMD	Duchenne muscular dystrophy
MedDRA	Medical Dictionary for Regulatory Activities
nmDBMD	nonsense mutation Duchenne and Becker muscular dystrophy
PDMS-2	Peabody Developmental Motor Scale (PDSM), Second Edition
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TESAE	Treatment Emergent Serious Adverse Event
TID	Three times per day
WHO	World Health Organization

1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the procedures and the statistical methods that will be used to analyze data and report results for PTC124-GD-016-DMD (Protocol Version 7.0: November 12, 2021).

This SAP will be approved prior to the final database lock.

1.1. Study Design

This study comprises an open-label, safety study of ataluren in subjects who previously received ataluren at an investigational site in a prior PTC-sponsored clinical study or treatment plan and siblings of those subjects.

This study will be performed at investigational sites in the US and Canada. It is planned that approximately 270 subjects will be enrolled. Subjects will receive ataluren 3 times per day (TID) at respective morning, midday, and evening doses of 10 mg/kg, 10 mg/kg, and 20 mg/kg. Study assessments will be performed during screening, on the first day of ataluren dosing, and then every 12, 24, and 48 weeks as described in Table 3.

For subjects from Study 048 only, study assessments will be performed, and motor development will be assessed using the PDMS-2 at baseline/Day 1, Week 14, and Week 28. After the Week 28 visit, study assessments will be performed every 12, 24, and 48 weeks from Week 40 as described in Table 4.

1.2. Study Objective and Endpoints

The objective of this study is to assess the safety (the primary endpoint) and tolerability of 10, 10, 20 mg/kg ataluren in subjects with nonsense mutation Duchenne and Becker muscular dystrophy (nmDBMD) who had prior exposure to ataluren in a PTC-sponsored clinical trial or treatment plan, and siblings of those patients (provided those patients have completed the placebo-controlled portion of the trial).

The safety profile of ataluren will be characterized by type, frequency, severity, timing, and relationship to ataluren of any adverse events (AEs) or laboratory abnormalities.

1.3. Sample Size Determination

The sample size for this study is based on the number of subjects in previous ataluren DMD studies and is not based upon any formal statistical hypothesis.

2. STUDY ANALYSIS SETS

2.1. As-Treated Population

The as-treated population consists of all subjects who receive at least 1 dose of ataluren. This population will be evaluated in the analysis of safety (the primary endpoint) and treatment administration.

3. GENERAL CONSIDERATIONS

3.1. General Considerations

The statistical evaluation will be performed by using the software package SAS release 9.4. Summary tables for continuous variables will contain the following statistics: n (number of subjects), mean, standard deviation, median, minimum, and maximum. In addition, changes from baseline will be likewise summarized.

Summary tables for categorical variables will include N (number of subjects in population), n (number of subjects in category), and percentage of subjects in category.

Assessments of change from baseline to post-treatment will include only those subjects with both baseline and post-treatment measurements.

3.2. Baseline

For each endpoint, baseline is defined as the last non-missing value before the first dose of study drug in PTC124-GD-016-DMD.

3.3. Analysis Visit

For all visits after the first dose of the study drug, unless otherwise stated, only the values recorded at scheduled time points will be used for analysis. However, unscheduled results will be included in tables reporting any abnormalities. All the measurements will be listed.

3.4. Missing Data Handling

All missing or partial data will be presented in the by-subject data listings as they are recorded on the Case Report Form (CRF). In general, missing or dropout data will not be imputed for the purpose of data analysis, unless otherwise specified.

4. SUBJECT DATA

4.1. Participant Dispositions

The disposition of subjects, including the number of subjects enrolled, number of subjects screen failed and reason for screen failures, subjects who prematurely discontinue study and the reason for the discontinuation will be tabulated for all screened subjects.

Disposition details will be presented in a by-subject data listing.

4.2. Demographic and Baseline Characteristics

Demographics and baseline characteristics including age, sex, race, ethnicity, country, height, weight, ambulatory status, and corticosteroid use (deflazacort, prednisone, or prednisolone) will be summarized for the as-treated population.

Demographic and Baseline characteristics will be presented in by-subject data listings.

4.3. Medical History

Medical history will be presented in a by-subject data listing.

4.4. Protocol Deviations

All major protocol deviations will be summarized for the as-treated population. A listing of protocol deviations will be presented for the as-treated population.

All major protocol deviations will be identified and documented by PTC team prior to database lock.

4.5. Duration of Treatment with Study Drug

Duration of treatment with study drug will be calculated as number of days from the date of the first dose to the date of the last dose of study drug, inclusive. Year is calculated as number of days divided by 365.25.

Duration of treatment will also be summarized by the following categories.

- <1 Year
- >=1 to <5 Years
- >=5 to <10 Years
- >=10 to <15 Years
- >=15 Years

Dose adjustment and reason for adjustment details will be presented in a by-subject data listing.

4.6. Study Drug Accountability

Study drug accountability details will be presented in a by-subject data listing.

4.7. Concomitant Medications and Supportive Therapy

All investigator terms for medications recorded on the CRF will be coded using the World Health Organization (WHO) Drug Dictionary (WHODrug-Global-B3 September 2025).

Prior medications will be defined as medications started prior to the first dose of study drug in PTC124-GD-016-DMD.

Concomitant medication will be defined as any medication other than ataluren, any treatments (including prescription and non-prescription drugs, health foods, herbal remedies, self-prescribed drugs, street drug, tobacco products, or alcohol) that are taken by a subject from the first dose of ataluren administration in PTC124-GD-016-DMD to 4 weeks after discontinuation of ataluren.

Any medication started before the first dose of study drug and continued at the time of first dose will be considered as both prior and concomitant medications.

Any medication with a partial or missing start date in which the prior medication status cannot be determined will be considered as a prior medication. Similarly, any medication with partial or missing end date in which the concomitant medication status for a period cannot be determined will be considered as a concomitant medication.

Prior and concomitant medication will be summarized by Anatomical Therapeutic Chemical (ATC) level 2 and preferred term (PT) for as-treated analysis set.

All the prior, concomitant medications and supportive therapy will be presented in a by-subject data listing.

5. SAFETY ANALYSES

All safety analyses will be based on the as-treated analysis set. Descriptive summaries will be based on nominal visits.

5.1. Adverse Events

Adverse events will be coded using the MedDRA (Version 28.1) classification system. The severity of AEs will be graded according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

A treatment-emergent adverse event (TEAE) is defined as an AE that occurs or worsens in the period extending from a subject's first ataluren dose in this study to 4 weeks after the last ataluren dose in this study.

An overview TEAE table, including number and percentage of subjects with TEAEs, treatment-emergent serious AEs (TESAEs), treatment-related TEAEs/TESAEs, TEAEs by maximum CTCAE grade, and TEAEs leading to discontinuation of study treatment will be provided.

The frequency of subjects experiencing a specific AE will be tabulated by System Organ Class (SOC) and Preferred Term (PT). Only TEAEs will be included in the summary tables.

The number and percentage of subjects will be tabulated for:

- Incidence of TEAEs by SOC and PT
- Incidence of TEAEs by PT in descending order
- Incidence of TEAEs by SOC, PT and maximum CTCAE grade
- Incidence of TEAEs with CTCAE Grade 3 or higher by SOC and PT
- Incidence of TEAEs by SOC, PT and relationship to study drug
- Incidence of TEAEs related to study drug by SOC and PT
- Incidence of TESAEs by SOC and PT
- TEAEs leading to discontinuation of study treatment by SOC and PT
- Incidence of TEAEs by SOC and PT will be summarized by duration of exposure categories (<1 Year, >=1 to <5 Years, >=5 to <10 Years, >=10 to <15 Years and >=15 Years)

Subjects who die, who have an SAE, and who have an AE leading to discontinuation of study treatment during the study will be listed in three separate data listings.

All AEs will be presented in a by-subject data listing.

5.2. Clinical Laboratory Parameters

Mean and mean change from baseline in clinical laboratory data listed in Table 1 will be summarized from baseline to last visit.

Table 1: Clinical Laboratory Parameters

Type	Parameters
Hematology	Cystatin C
Biochemistry	Alanine Aminotransferase, Aspartate Aminotransferase, Creatine Kinase
Urinalysis	Creatinine

The criteria of laboratory parameters to monitor renal abnormalities are presented in Table 2. A summary table will be generated to count the incidence of criteria met for post-baseline results.

Table 2: Renal Monitoring Parameters and Actions to Be Taken

Laboratory Parameter	Stop Study Drug Immediately, Confirm Abnormal Value, and Then Start Work-Up	Stop Study Drug After Confirming[a] Abnormal Value, and Then Start Work-Up
Serum cystatin C	>2.00 mg/L	>1.33-2.00 mg/L
Serum creatinine	≥ Grade 2 (≥1.5 x ULN for age)	Grade 1 (>ULN - 1.5 x ULN for age)
Serum BUN	≥3.0 x ULN	≥1.5-3.0 x ULN

Abbreviations: BUN, blood urea nitrogen; ULN, upper limit of normal
[a] Laboratory abnormalities may be confirmed immediately or at the next scheduled clinic visit based on investigator judgment.

5.3. Vital Signs

Vital signs (including systolic and diastolic blood pressure, radial pulse rate, body temperature, height, and weight) data will be presented in a by-subject data listing.

5.4. Physical examinations

Physical examination findings will be presented in a by-subject data listing.

5.5. Peabody Developmental Motor Scale, Second Edition *(*PDMS-2)

The PDMS-2 is a validated instrument used to measure motor skills and developmental milestone achievement in infants and children (Folio 2000), which will only be performed in subjects entering the study from Study 048.

The PDMS-2 assessments will be provided in a by-subject data listing for subjects enrolled from Study 048.

6. CHANGES FROM THE PROTOCOL

The duration of the concomitant medication and TEAE upper bound was adjusted from 6 weeks to 4 weeks following the last ataluren dose in this study.

Laboratory data will not be graded or summarized by CTCAE severity grade, as clinically significant lab results will be recorded as adverse events, thereby fulfilling the safety monitoring requirements.

7. REFERENCES

Folio, M and Fewell, R. Peabody Developmental Motor Scales. 2nd Edition. Texas: PRO-ED 2000.

8. MOCK TABLES, LISTINGS, AND GRAPHS

The tables, listings, and graphs shells for the study will be provided in a separate document.

9. VERSION HISTORY

SAP Version	Approval Date	Change	Rationale
1.0	21 NOVEMBER 2025	Not Applicable	Original version

APPENDIX 1. SCHEDULE OF EVENTS

Table 3: Schedule of Events

Study Period	**Screening**	**Baseline**	**Treatment**				**6 Weeks Post D/C**
Study Week (±7 Days)	**Day 1[a]**	**Day 1[a]**	**Every 12 Weeks**	**Every 24 Weeks**	**Every 48 Weeks[b]**	**End of TX**	
Informed consent[c]	X	X					
Clinical history[d]	X	X					
Vital signs	X				X	X	X
Height	X						
Weight	X	X		X[e]	X	X	X
Physical examination	X						
Hepatitis B and C[f]	X						
Hematology	X				X	X	X
Biochemistry	X				X	X	X
Drug dispensed		X	X[g]	X[g]	X[g]		
Pre-/post-shipment communication			X[h]	X[h]	X[h]		
Drug compliance			X[i]	X[i]	X[i]	X	
Adverse events	X	X	X[j]	X[j]	X[j]	X	X
Concomitant medication	X	X	X[j]	X[j]	X[j]	X	X

Abbreviations: D/C, discontinuation; TX, treatment

[a] Subjects who have not participated in an ataluren study in the past year are required to complete all assessments identified under screening. Subjects who have participated in an ataluren study within the past year only need to compete the assessments identified under baseline.

[b] Annual visits will occur every 48 weeks (ie, Weeks 48, 96, 144, 192, 240, 288, 336, 384, 432, 480, 528, 576, 624, 672, 720, etc).

[c] Informed consent will be signed before any study procedures are performed.

[d] Clinical history will be collected for ataluren-naïve subjects (siblings). For subjects enrolling from another ataluren clinical study, only clinical history reported since the last dose of ataluren in the prior DMD study will be collected.

[e] Reminders will be communicated prior to every 24 week visit for subject to obtain a weight check-in between the annual visits at sites. This communication will be documented in the source.

[f] Hepatitis B and C testing is only required for ataluren-naïve subjects (siblings) or subjects who have a temporary treatment gap of 1 year before entering Study 016.

[g] Drug will be dispensed to the subject every 12 weeks.

[h] Clinical site staff will contact the subject or parent(s)/legal guardian(s) to confirm details and timing of the upcoming study drug shipment. Post-shipment contact will confirm receipt of and condition of study drug.

[i] Subjects or parent(s)/caregiver(s) or legal guardian(s) should return all used and unused cartons and unused sachets of ataluren as instructed in order to assess study drug compliance.

[j] Clinical site staff will contact subject or parent(s)/legal guardian(s) every 12 weeks (by phone, email, or text if there is no clinic visit) to assess adverse events and concomitant medications.

Table 4: Schedule of Events for PTC124-GD-048-DMD Subjects

Study Period	Scr/Baseline	Treatment						6 Weeks Post D/C
Study Week (±7 Days)	Day 1[a]	Week 14[b]	Week 28[b]	Week 40 Through End of TX				
				Every 12 Weeks[c]	Every 24 Weeks[c]	Every 48 Weeks[c]	End of TX	
Informed consent[d]	X							
Clinical history[e]	X							
Vital signs	X		X			X	X	X
Height	X	X	X					
Weight	X	X	X		X[f]	X	X	X
Physical examination	X							
Hepatitis B and C[g]	X							
Hematology		X	X			X	X	X
Biochemistry		X	X			X	X	X
Drug dispensed	X	X[h]	X[h]	X[i]	X[i]	X[i]		
Pre-/post-shipment communication		X		X[j]	X[j]	X[j]		
Drug compliance	X	X	X	X[k]	X[k]	X[k]	X	
Adverse events	X	X	X	X[l]	X[l]	X[l]	X	X
Concomitant medication	X	X	X	X[l]	X[l]	X[l]	X	X
PDMS-2	X	X	X					

Abbreviations: D/C, discontinuation; PDMS-2, Peabody Developmental Motor Scale, second edition; Scr, screening; TX, treatment

[a] Screening/baseline (Day 1) of the current study may be the same day as visit 5 (Week 24) in Study PTC124-GD-048-DMD, in which case, corresponding assessments in the two studies do not need to be repeated.

[b] Weeks 14 and 28 of the current study represent 38 and 52 weeks, respectively, of ataluren treatment for these Study 048 subjects.

[c] After the Week 28 visit, assessments will be conducted as outlined in the table every 12 weeks, every 24 weeks, and every 48 weeks. These visits will be anchored by the visit date for Week 28. The visit following Week 28 should be the first every 12 week visit at approximately Week 40 post-enrollment. Annual visits will occur every 48 weeks (ie, Weeks 76, 124, 172, etc).

[d] Informed consent will be signed before any study procedures are performed.

[e] Clinical history reported since the last dose of ataluren in Study 048 will be collected.

[f] Reminders will be communicated prior to every 24 week visit for subject to obtain a weight check-in between the annual visits at sites. This communication will be documented in the source.

[g] Hepatitis B and C testing is only required for ataluren-naïve subjects (siblings) or subjects who have a temporary treatment gap of 1 year before entering Study 016.

[h] Drug will be dispensed manually at the Week 14 and Week 28 visits.

[i] After the Week 28 visit, drug will be dispensed to the subject every 12 weeks.

[j] Clinical site staff will contact the subject or parent(s)/legal guardian(s) to confirm details and timing of the upcoming study drug shipment. Post-shipment contact will confirm receipt of and condition of study drug.

[k] Subjects or parent(s)/caregiver(s) or legal guardian(s) should return all used and unused cartons and unused sachets of ataluren as instructed in order to assess study drug compliance.
[l] Clinical site staff will contact subject or parent(s)/legal guardian(s) every 12 weeks (by phone, email, or text if there is no clinic visit) to assess adverse events and concomitant medications.

Signature Page for PTC124-GD-016-DMD Statistical Analysis Plan (SAP) V1.0 - 21NO

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