NCT #: NCT04632940

STATISTICAL ANALYSIS PLAN

PROTOCOL TITLE:	A Phase 3, Randomized, Double-Blind, Trial of Pamrevlumab (FG-3019) or Placebo in Combination with Systemic Corticosteroids in Ambulatory Subjects with Duchenne Muscular Dystrophy (DMD)
PROTOCOL NUMBER:	Protocol FGCL-3019-094 (OLE)
PROTOCOL AMENDMENT VERSION:	4.0 (28 October 2022)
STUDY SPONSOR:	FibroGen, Inc. 409 Illinois Street San Francisco, California 94158 USA
STUDY DRUG:	Pamrevlumab
INDICATION:	Duchenne Muscular Dystrophy (DMD)
SAP VERSION:	Final V1.0 (Part 2 - OLE Period)

SIGNATURE PAGE

Approvals

I have reviewed and accepted the information in this document to be a true and accurate representation of the Statistical Analysis Plan.

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Signatory	Significance
Initiator	By signing, the author is attesting that the content of the document is complete and accurate.
Reviewer	By signing, the reviewer is attesting that the document's approach and contents are compliant with the study protocol, all appropriate, regulatory requirements, and other significant guidelines. This individual(s) has reviewed the document for accuracy and completeness.

CHANGE HISTORY

Version	Date	Description
1.0	18Dec2023	Final approved version

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LIST OF ABBREVIATIONS

Abbreviation	Definition
4SCV	4-Stair Climb Velocity
ADA	Antidrug Antibody
AE	Adverse Event
BSA	Body Surface Area
DMD	Duchenne Muscular Dystrophy
DMC	Data Monitoring Committee
FG-3019	FibroGen-3019 (Recombinant Human Monoclonal Antibody), Pamrevlumab
IGS	Immunogenicity Analysis Set
IV	Intravenous
LoA	Loss of Ambulation
MMRM	Mixed Model for Repeated Measures
NAb	Neutralizing Antibody
NSAA	NorthStar Ambulatory Assessment
OLE	Open Label Extension
PEY	Patient Exposure Years
SAF	Safety Analysis Set
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment Emergent Adverse Event
TESAE	Treatment Emergent Serous Adverse Event
TLF	Tables, Listings, and Figures
TTSTAND	Time to Stand

1. INTRODUCTION

This statistical analysis plan (SAP) is for the pre-specified reporting of study results for protocol FGCL-3019-094, amendment 4.0. Specifications of tables, data listings, and figures (TLFs) are contained in a separate document. This is Part 2 of the SAP, which documents the planned analyses for the open-label extension (OLE) period. For the purposes of this document, references to Part 1 of the SAP refer to the SAP for the randomized, placebo-controlled portion of the study.

In this document, only new definitions and rules will be described; the same definitions and rules described in the SAP for the main study will not be repeated.

2. STUDY OBJECTIVE

The overall objective of this Phase 3 registration-enabling study is to evaluate the efficacy and safety of 35 mg/kg intravenous (IV) infusions of pamrevlumab as compared to placebo in ambulatory subjects with Duchenne Muscular Dystrophy (DMD) over 52 weeks. The objective of the optional open-label, single arm extension is to evaluate long-term efficacy and safety of pamrevlumab in DMD subjects.

3. STUDY DESIGN (OLE PERIOD)

3.1. Enrollment to OLE Period

Subjects who complete the Week 52 visit of the main study (regardless of the number of study drug infusions received) will be eligible to participate in the optional OLE period of the study that offers continuing access to pamrevlumab regardless of randomization assignment in the main study. Subjects will be considered as having entered the OLE study if they have received at least one dose of the study drug during the OLE period.

3.2. Randomization

Randomization is not applicable for the OLE period. All patients will receive IV pamrevlumab 35 mg/kg.

3.3. Study Periods

- **Optional, OLE period of pamrevlumab:**
    - Access to pamrevlumab will be available until the last subject completes 52 weeks of treatment in the OLE period, or pamrevlumab is commercially available, or the Sponsor decides to end the OLE period, whichever occurs first.
- **Follow-up period/final safety assessments:**
    - 28 days after the last dose
    - 60 days after the last dose: follow-up phone call, for a final safety assessment

4. STUDY ENDPOINTS (OLE)

The following efficacy and safety assessments will be collected only as standard-of-care per each investigational site's real-world practice and descriptively presented during the OLE period:

Efficacy assessments:

- Change in NorthStar Ambulatory Assessment (NSAA) total score
- Change in 4-stair climb Velocity (4SCV) assessment
- Change in the 10-meter walk/run test
- Change in Time to Stand (TTSTAND)
- Time of Loss of Ambulation (LoA) assessment
- Cumulative Loss of Function Analysis for NSAA
- Proportions of subjects in 10-meter walk/run test > 10 seconds

Safety assessments:

- Treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), clinically significant laboratory test abnormalities, discontinuation of treatment due to TEAEs, and hypersensitivity/anaphylactic reactions
- Number and percentage of subjects with hospitalizations due to any serious adverse events with pulmonary and/or cardiac cause(s)
- Number and percentage of subjects with bone fractures
- Annualized height velocity from Baseline of OLE

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. Statistical Methodology

All data collected will be included in the data listings. All analyses will be performed using SAS® Version 9.4 or higher.

5.1.1. Analysis of Categorical Endpoints

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

5.1.2. Analysis of Continuous Endpoints

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

5.1.3. Analysis of Time-to-Event Endpoints

Kaplan-Meier curves for time-to-event endpoints will be plotted as appropriate.

5.1.4. Analysis of Spirometry Data

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

5.2. Analysis Set

The **Safety Analysis Set - OLE (SAF-OLE)** includes all subjects who have received at least one study medication in the OLE period. Subjects will be analyzed according to the previous treatment actually received in the main study.

All analysis in OLE will be performed on SAF-OLE unless otherwise specified.

The **Immunogenicity Analysis Set (IGS)** contains all the antidrug antibody (ADA) evaluable patients, who are in the SAF-OLE analysis set with at least one ADA/neutralizing antibody (NAb) sample (with reportable results) taken pre-treatment (i.e., a baseline sample) and at least one ADA sample (with reportable result) taken post-treatment in the OLE period.

5.3. General Data Handling Rules and Presentation Specifications

5.3.1. Analysis Period

- The safety analysis will be based on the on-study period which is defined as from Day 1 in the OLE period up to the end of the entire study, regardless of patients' treatment status.
- Efficacy analyses will be based on the entire study period which includes both the main study period and the OLE period.

5.3.2. Baseline Definitions

- Baseline for the OLE period is defined as the last acceptable assessment on or prior to the first dosing date in the OLE period.
- Baseline for main study period is defined the same as in SAP Part 1 for the randomized treatment period.

5.3.3. Formulas

- Study Day Calculation
  - The day when a subject receives the first dose of study drug in the OLE period is designated as Day 1 in OLE.
  - Study day of an assessment/procedure is calculated as follows.
    - For assessments or procedures on Day 1 or later,

      Study day = assessment/procedure date – Day 1 date + 1.

    - For assessments or procedures earlier than Day 1,

      Study day = assessment/procedure date – Day 1 date.

- Follow the same formulas as described in SAP Part 1 for the randomized treatment period:
  - Body surface area (BSA)
  - Change from Baseline
- Patient exposure years (PEY) (on pamrevlumab in OLE period)
  - PEY = Number of subjects × Average Duration of Exposure (year), where duration of exposure for each subject is (date of last non-zero dose on pamrevlumab – date of first dose in OLE period on pamrevlumab + 1)/365.25.

5.3.4. General Instructions of TLF

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

Summary tables will be presented for each treatment group in the main study and all subjects pooled in the OLE period.

Long-term efficacy data will be analyzed during the entire study period which includes both the main study period and the OLE period and safety data will be summarized only in the OLE period for subjects who entered OLE and got dosed.

5.3.5. Handling Dropouts and Missing Data

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

5.4. Interim Analysis and Data Monitoring Committee

In addition to routine safety monitoring, an independent Data Monitoring Committee (DMC) will be established to review safety data on an ongoing basis. A DMC charter will establish the procedures, meeting frequency, and scope of responsibilities of the committee.

This study has no planned or pre-specified interim analysis for either efficacy or futility.

6. STATISTICAL ANALYSIS

6.1. Subject Accountability and Disposition

The number (%) of subjects who entered the OLE period, discontinued prematurely from treatment, discontinued prematurely from study, and reasons for premature discontinuation will be presented for each previous treatment group in the main study and all subjects pooled.

Enrollment will also be summarized by study site.

6.2. Protocol Deviations

The number and percentage of subjects with important protocol deviations will be categorized and tabulated as appropriate. COVID-19 related important protocol deviations will be summarized in a separate table. All protocol deviations will be finalized prior to database lock.

6.3. Demographics and Baseline Characteristics

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

6.4. Medical History

Medical history summary will be presented for the OLE period.

6.5. Concomitant Medications

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period. No prior medications summary will be presented.

6.6. Treatments and Medications

6.6.1. Study Drug Exposure

Study treatment will be summarized for the main study, OLE period, and entire study, respectively. SAF-OLE in the main study will be used for summaries of the main study and the entire study (Main + OLE Periods).

- Duration of exposure in Main Study = date of last non-zero dose in Main Study– date of the first dose in Main Study + 1.
- Duration of exposure in the OLE period = date last non-zero dose in the OLE period – date of the first dose in the OLE period + 1.
- Duration of entire study treatment exposure (Main + OLE Periods) = date last non-zero dose in study – date of the first dose in study + 1.

Duration of study treatment in the OLE period will be summarized as a continuous variable and be tabulated by the categories as follows:

- <26 Weeks
- 26 to <52 Weeks
- 52 to <78 Weeks
- 78 to <104 Weeks
- 104 to <130 Weeks
- ≥130 Weeks

Number of infusions is defined as the number of non-zero dose infusions.

The following dose administration parameters:

- Total number of infusions in the OLE period (≤12, 13-24, 25-36, 37-48, 49-60, >60)
- Overall average infusion doses (in mg/kg) in the OLE period
- Whether infusion was interrupted and reason for interruption in the OLE period

6.6.2. Treatment Compliance

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period.

Compliance will be derived for the main study, OLE period, and entire study, respectively.

6.7. Efficacy Analysis

All analyses for efficacy endpoints will be performed for the SAF-OLE during the on-study period unless noted otherwise.

6.7.1. Primary Endpoint Estimand and Analysis

6.7.1.1. Estimand Strategy

The primary estimand is intended to provide a population-level efficacy assessment of the pamrevlumab on a continuous endpoint, regardless of participant compliance with the investigational product dosing.

6.7.1.2. Population of Interest

All subjects in SAF-OLE.

6.7.1.3. Intercurrent Event Handling Strategy

Treatment policy strategy will be used for any intercurrent event. No imputation on missing data.

6.7.1.4. Analysis Variable

Change from baseline in all NSAA assessments (scheduled and unscheduled) in the OLE period, including scheduled, unscheduled, and available assessments after treatment discontinuation, will be included in the analysis.

6.7.1.5. Population Summary for Treatment Comparison

Efficacy parameters, including change from baseline in 4SCV, the 10-meter walk/run test, TTSTAND, Time of LoA, and proportions of subjects in 10-meter walk/run test >10 seconds will be analyzed at Week 24, Week 36, and Week 48 in the OLE period using Mixed Model for Repeated Measures (MMRM) approach with fixed effects for treatment, visit (as a factor), treatment-by-visit interaction, and covariates (baseline values). The results at each analysis visit from baseline of the main study till the last visit with evaluable assessments in the OLE period will be presented.

6.8. Safety Analysis

The safety analyses will be performed for the SAF-OLE in the OLE period.

6.8.1. Adverse Events (AE)

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period with additional PEY for OLE period on pamrevlumab provided.

6.8.2. Clinical Laboratory Parameters

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period. The analysis visit window is defined in Appendix 1.

6.8.3. Vital Signs

Follow the same guidelines as described in SAP Part 1 for the randomized treatment period. The analysis visit window is defined in Appendix 1.

6.9. Immunogenicity Analysis

Analysis of immunogenicity data will be based on IGS. Analysis dataset and data listing will include all available ADA samples. The following terms and definitions are implemented.

6.9.1. Terms and Definitions

6.9.1.1. Sample ADA Status:

- Baseline ADA-positive sample: ADA is detected in the last sample before initiation of treatment.
- Baseline ADA-negative sample: ADA is not detected in the last sample before initiation of treatment.
- **Treatment-emergent ADA-Positive**: Meets definition of treatment-induced or treatment-boosted ADA. After initiation of treatment,
  - **Treatment-induced ADA-Positive**: A post-treatment positive ADA is detected in a subject for whom pre-treatment ADA assessment is either negative or not assessable, or
  - **Treatment-boosted ADA-Positive**: Pre-existing ADA were boosted to a higher-level following study treatment, i.e., pre-treatment positive ADA titer was boosted by at least 2 dilution steps (4-fold) following study treatment.
- ADA-negative sample: After initiation of treatment, ADA is not treatment-emergent ADA-positive.

Next, using the sample ADA status, subject ADA status is defined.

6.9.1.2. Subject ADA Status:

- Baseline ADA-positive subject: A subject with baseline ADA-positive sample.
- ADA-positive subject: An evaluable subject with at least one treatment-emergent ADA sample at any time during the study.
- Neutralizing-positive: At least one treatment-emergent ADA-positive sample with neutralizing antibodies detected (if available).
- ADA-negative subject: An evaluable patient without a treatment-emergent ADA-positive sample during the study.

6.9.2. Statistical Analysis for Characterization of ADA Immune Response

6.9.2.1. Incidence of ADA

- Percentage of treatment-emergent ADA patients for the defined study period, where the denominator is the number of ADA evaluable patients in the respective treatment arm and/or subgroup.
- Number (%) of subjects will be reported for the following parameters based on evaluable subjects:
  - Baseline ADA-positive
  - ADA-positive (Treatment-induced, Treatment-boosted)
  - Neutralizing Positive (if available)
  - ADA-negative
- **ADA prevalence**: Percentage of treatment-emergent ADA patients at any given timepoint, where the denominator is the number of ADA evaluable patients in the respective treatment arm and/or subgroup at that timepoint.
- A listing of all ADA assessments will be provided.
- Additionally, a separate listing of ADA assessments for all NAb-positive subjects will be provided (if available).

6.9.2.2. ADA Titer Kinetics

All ADA-positive subjects will be included in the analysis.

- Summary statistics of subject-level ADA titers using the maximum titer value within an ADA positive subject will be presented for baseline ADA-negative subjects and baseline ADA positive subjects. The median, mean (standard deviation [SD]), interquartile range, range of the maximum titers, and geometric mean (SD) will be reported. For ADA-positive subjects with baseline ADA-positive sample, the median and interquartile range of the fold increase from baseline in titer (ratio of maximum post-baseline titer to baseline titer) will also be reported. Graphical presentation of the summary data may be provided using boxplots, as appropriate.
- For sample-level ADA titers, boxplots of ADA titers at each assessment timepoint will be provided, as appropriate, to demonstrate whether the ADA levels tend to change over time during the treatment, along with ADA incidence at each assessment timepoint.
- Spider plots may be considered to show the trend of ADA titer over time for subjects with ≥ 5 ADA results by splitting subjects into multiple spider plots (eg, $\approx \leq 10$ per plot, approximately.

7. CHANGES FROM PROTOCOL

- Cumulative loss of function analysis (Section 4) was added as an efficacy endpoint.
- Proportions of subjects in 10-meter walk/run test was added as an efficacy endpoint.
- Annualized height velocity from Baseline of OLE was not analyzed due to the limited collection of data.

8. REFERENCE

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9. APPENDICES

APPENDIX 1. ANALYSIS VISIT WINDOWS

Analysis visits are defined by the windows that will have the widths of the corresponding assessments centered at the scheduled time. Unscheduled visits within a visit window defined below will be grouped into the closest scheduled visits based on the visit date.

Table 1: Analysis Visit Window for Vital Signs

Analysis Visit	Target Day in OLE	Start Day	End Day
Baseline	See Section 5.3.2		
EX-Day 1	1	1	1
EX-Week k K=1,2,3,…	7*2k+1	$(\text{End Day})_{k-1}$+1	7*2k+8

Table 2: Analysis Visit Window for MFT and Weight*

Analysis Visit	Target Day	Start Day	End Day
Baseline	See Section 5.3.2		
EX-Day 1	1	1	1
EX-Week k K=1,2,3,…	7*12k+1	$(\text{End Day})_{k-1}$+1	(7*12k+1)+12*7/2

* Weight is collected during the dose adjustment visit or can be done up to two weeks in advance.

Table 3: Analysis Visit Window for Labs, and Physical Examinations

Analysis Visit	Target Day	Start Day	End Day
Baseline	See Section 5.3.2		
EX-Day 1	1	1	1
EX-Week k K=1,2,3,…	7*24k+1	$(\text{End Day})_{k-1}$+1	(7*24k+1)+24*7/2

Table 4: Analysis Visit Window for Immunogenicity Data

Analysis Visit	Target Day	Start Day	End Day
Baseline	Assessment prior to first dose in OLE		

EX-Week k K=1,2,3,…	7*24k+1	$(\text{End Day})_{k-1}+1$	(7*24k+1)+24*7/2

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Statistical Analysis Plan

TITLE PAGE

PROTOCOL TITLE:	A Phase 3, Randomized, Double-Blind, Trial of Pamrevlumab (FG-3019) or Placebo in Combination with Systemic Corticosteroids in Ambulatory Subjects with Duchenne Muscular Dystrophy (DMD)
PROTOCOL NUMBER:	Protocol FGCL-3019-094 Amendment 4: 28 October, 2022
STUDY SPONSOR:	FibroGen, Inc. 409 Illinois Street San Francisco, California 94158 USA
STUDY DRUG:	Pamrevlumab
INDICATION:	Duchenne Muscular Dystrophy (DMD)
SAP VERSION	Final 2.0
RELEASE DATE	9 August, 2023

SIGNATURES AND APPROVALS

Approvals

I have reviewed and accepted the information in this document to be a true and accurate representation of the Statistical Analysis Plan.

Initiator:

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Signature Significance

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Signatory	Significance
Initiator	By signing, the author is attesting that the content of the document is complete and accurate.
Reviewer	By signing, the reviewer(s) are attesting that the document's approach and contents are compliant with the study protocol, all appropriate, regulatory requirements, and other significant guidelines. This individual(s) has reviewed the document for accuracy and completeness.

CHANGE HISTORY

Version	Date	Description
Final 1.0	25JUL2023	Initial version
Final 2.0	9AUG2023	Removed analysis related to biceps brachii because it is not included in the protocol. Added a statement on the baseline definition for MFT assessments in "Changes from Protocol" section. Replaced "infusion-related reactions" with "infusion reactions".

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LIST OF ABBREVIATIONS

Abbreviation	Definition
ADA	Anti-Drug Antibody
ADaM	Analysis Data Model
AE	Adverse Event
ALT	Alanine Aminotransferase
ANCOVA	Analysis of Covariance
AST	Aspartate Aminotransferase
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BSA	Body Surface Area
CBC	Complete Blood Count
CDE	Center for Drug Evaluation (China)
CRF	Case Report Form
CS	Clinically Significant
CSR	Clinically Study Report
CTCAE	Common Terminology Criteria for Adverse Events
DBL	Database Lock
DMD	Duchenne Muscular Dystrophy
DMC	Data Monitoring Committee
DVA	Duchenne Video Assessment
ECG	Electrocardiogram
EOS	End of Study
EOT	End of Treatment
FG-3019	FibroGen-3019 (Recombinant Human Monoclonal Antibody), Pamrevlumab
HAHA	Human Anti-Human Antibody
IP	Investigational Product
ITT	Intent-to-Treat
IV	Intravenous
LLN	Lower Limit of Normal
LoA	Loss of Ambulation
LVEF%	Left Ventricular Ejection Fraction Percentage

Abbreviation	Definition
MedDRA	Medical Dictionary for Regulatory Activities
MFT	Muscle Function Tests
MI ANCOVA	Multiple Imputation ANCOVA
MMRM	Mixed Model Repeated Measures
MRI	Magnetic Resonance Imaging
Nab	Neutralizing Antibody
NCI	National Cancer Institute
NSAA	North Star Ambulatory Assessment
OLE	Open Label Extension
PD	Pharmacodynamics
PFT	Pulmonary Function Test
PK	Pharmacokinetic
ppFVC	Percent Predicted Forced Vital Capacity
ppPEF	Percent Predicted Peak Expiratory Flow
PT	Preferred Term
aPTT	Activated Partial Prothrombin Time
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDTM	Study Data Tabulation Model
SE	Standard Error
SoA	Schedule of Assessments
SOC	System Organ Class
TEAE	Treatment-emergent Adverse Event
TESAE	Treatment-emergent Serous Adverse Event
TFLs	Tables, Figures and Listings
TTSTAND	Time to Stand (from Supine)
ULN	Upper Limit of Normal
WHODD	World Health Organization Drug Dictionary
4SCV	4-Stair Climb Velocity

1. INTRODUCTION

This statistical analysis plan (SAP) provides a more technical and detailed elaboration of the statistical analyses of study data as specified in the Study Protocol FGCL-3019-094 Amendment 4, 28 October 2022. Specifications of tables, figures, and listings (TFLs) are contained in a separate document. The statistical analyses and summary tabulations described in this SAP provide the basis for the results sections of the clinical study report (CSR) for this study. The SAP will be finalized and signed off prior to database lock (DBL). Any major modification of this SAP after the signoff will be documented in a SAP amendment or the CSR.

This SAP is only for the main study period. The Open Label Extension (OLE) will have a separate SAP. A population pharmacokinetic (PK) analysis, as well as an exposure-response analysis, will be defined in a separate PK analysis plan.

Based on regional regulatory filing needs, region specific populations will be analyzed following this same SAP. Refer to Appendix 6 if regulatory submission in China is pursued.

2. STUDY OBJECTIVES

The overall objective of this trial is to evaluate the efficacy and safety of pamrevlumab versus placebo in combination with systemic corticosteroids administered every two weeks in ambulatory subjects with Duchenne muscular dystrophy (age 6 to <12 years).

3. STUDY DESIGN

3.1. Overview

Study FGCL-3019-094 is a Phase 3, randomized, double-blind, placebo-controlled multi-center trial to evaluate the efficacy and safety of pamrevlumab in ambulatory subjects with DMD over a 52-week period.

3.2. Study Population

Approximately 70 subjects will be enrolled in this trial, globally.

3.3. Sample Size Determination

With a total sample size of 70 subjects allocated in a 1:1 ratio between the pamrevlumab arm and the placebo arm, the study will achieve at least 80% power to detect an effect size of 0.705 (assuming a treatment difference of 6.0 points in linearized total North Star Ambulatory Assessment [NSAA] with common standard deviation of 8.5, or a treatment difference of 1.91 in raw total NSAA with common standard deviation of 2.71) in the mean change from baseline in the total score of NSAA with a one-sided significance level (alpha) of 0.025.

3.4. Randomization and Treatment Assignment

Subjects will be randomized by a 1:1 ratio to one of the two study treatment arms as follows:

- Arm A: pamrevlumab 35 mg/kg IV Q2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally.
- Arm B: matching placebo IV Q2 weeks + systemic deflazacort or equivalent potency of corticosteroids administered orally.

Randomization will be stratified by exon 44 deletion (Yes/No).

3.5. Study Periods

This study consists of the following study periods (Figure 1):

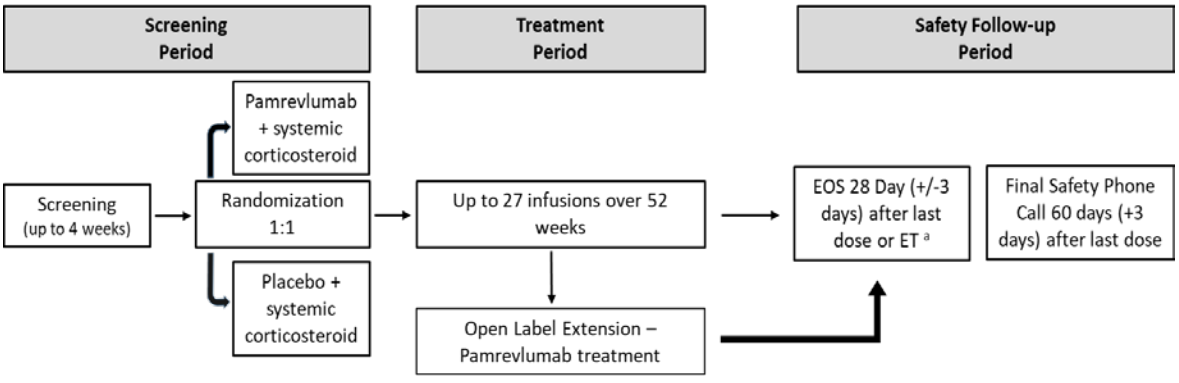
- Main (double-blind, placebo-controlled) study period:
  - Screening period: Up to 4 weeks
  - Treatment period: 52 weeks
- Optional, open label extension (OLE) period:

  Subjects who complete week 52 of the main study (regardless of the number of study drug infusions received) will be eligible to participate in the OLE where all subjects will be treated with pamrevlumab. If a subject discontinues the main study early for any reason they will not be eligible for inclusion in the OLE.
- Follow-up period/final safety assessment:
  - 28 days after last dose: scheduled visit
  - 60 days after last dose: follow-up phone call, for a final safety assessment

Subjects who discontinue study treatment for any reason will be encouraged to return to the investigative site to complete final safety and efficacy assessments.

A schematic overview of the study is provided in Figure 1. A detailed overview of assessments and the timing of assessments are provided in Appendix 1.

Figure 1: FGCL-3019-094 Study Schema



Abbreviations: EOS= End of Study, ET=Early Termination
a) Subjects who discontinue the study early, for any reason, will complete an early termination visit 28 days (+/- 3 Days) and a final safety follow-up phone call 60 days (+ 3 days) after the last infusion.

3.6. Study Assessments

The intent of this study is to evaluate the efficacy and safety profile of pamrevlumab in combination with systemic corticosteroids in subjects with ambulatory Duchenne muscular dystrophy (age 6 to <12 years).

The following assessments will be assessed by following the schedules defined in the protocol (SoA in the Appendix of the protocol).

- North Star Ambulatory Assessment (NSAA)
- 4-Stair Climb Velocity (4SCV)
- 10-Meter Walk/Run Test
- Time to Stand (TTSTAND)
- Time to Loss of Ambulation (LoA)
- Duchenne Video Assessment (DVA)
- Percent predicted FVC (ppFVC) and percent predicted Peak Expiratory Flow (ppPEF) assessed by spirometry
- Lower extremities vastus lateralis muscle fibrosis score assessed by magnetic resonance imaging (MRI)

Safety assessments will be assessed throughout the study and in accordance with the SoA in the protocol, including but not limited to, adverse events (AEs), concomitant medications, laboratory tests, vital signs, and physical exams.

In addition, an independent Data Monitoring Committee (DMC) will review safety and other clinical data (with the authority to unblind such data if deemed necessary) on a periodic basis to monitor overall subject safety.

4. STUDY ENDPOINTS

4.1. Primary Endpoint

- Change in the total score of North Star Ambulatory Assessment (NSAA) from baseline to Week 52

4.2. Secondary Endpoints

- Change in 4-stair climb Velocity (4SCV) assessment from baseline to Week 52
- Change in 10-meter walk/run test from baseline to Week 52
- Change in TTSTAND from baseline to Week 52
- Time to Loss of Ambulation (LoA) from baseline to Week 52
- Proportions of subjects in 10-meter walk/run test at Week 52

4.3. Safety Assessments

- All treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events (TESAEs), clinically significant laboratory test abnormalities, discontinuation of treatment due to treatment-related AEs and hypersensitivity/anaphylactic reactions
- Number and percentage of subjects with hospitalizations due to any serious adverse events (SAEs) with pulmonary and/or cardiac cause(s), after the first dose of investigational product (IP)
- Number and percentage of subjects with bone fractures
- Annualized height velocity (cm/year) from Baseline to Week 52

4.4. Exploratory Endpoints

- Change in DVA severity percentage from baseline to Week 52
- Change in ppFVC and ppPEF assessed by spirometry, from baseline to Week 52
- Changes in lower extremities vastus lateralis muscle fibrosis score from baseline to Week 52, assessed by MRI

4.5. Pharmacokinetics/pharmacodynamics (PK/PD) assessment

- Population PK/PD analysis

5. GENERAL STATISTICAL CONSIDERATIONS

5.1. General Conventions

All analyses will be performed using SAS® Version 9.4 or higher. All data collected will be presented by data listings for review and substantiation of summary tables.

5.1.1. Analysis for Categorical Endpoints

Frequency distributions (number and percentage of subjects) will be presented for categorical variables.

For categorical variables, the confidence interval (CI) of proportions for each treatment group will be calculated using the Clopper-Pearson method as appropriate. The SAS PROC FREQ procedure with BINOMIAL (EXACT) statement will be used to provide the Clopper-Pearson exact 95% CIs for proportions. Bar graphs of proportions for categorical variables will be plotted as appropriate.

5.1.2. Analysis for Continuous Endpoints

For continuous variables, descriptive statistics, including n, mean, standard deviation (SD), median, minimum, and maximum, will be presented. Unless otherwise stated, all confidence intervals will be two-sided 95% confidence intervals.

For select continuous variables, line graphs of group mean (and standard error [SE]) and mean change from baseline (and SE) values will be plotted over visits.

Baseline characteristics, safety, efficacy, and other data will be summarized by treatment arm based on available data in the Intent-to-Treat (ITT)/Safety Analysis Set, except for the variables specifically indicated otherwise. Baseline tables will include an Overall group and inter-quartiles (Q1, Q3) for descriptive statistics.

Efficacy and safety analyses for treatment comparisons will be based on data observed during the main study period (52 weeks). Data from the OLE period will be summarized descriptively.

The statistical comparisons will be performed between treatment groups as deemed appropriate. The treatment groups will be presented as follows:

- Pamrevlumab
- Placebo

5.2. Analysis Sets

The following analysis sets will be used for statistical analysis:

5.2.1. Intent-to-Treat Set (ITT)

The ITT set will include all randomized subjects. Subjects will be analyzed according to their randomized treatment arm.

5.2.2. Per-Protocol Set (PPS)

The per-protocol set will be defined as all randomized subjects who completed at least 24 doses of treatment, with baseline and at least one post-baseline NSAA assessments, did not early terminated from treatment or study, and no major protocol deviation(s) that significantly impact efficacy analyses.

5.2.3. Safety Analysis Set (SAF)

The safety analysis set will include all subjects who receive any dose of study medication. All safety data will be analyzed using the SAF. Subjects will be analyzed according to the treatment actually received.

5.2.4. Immunogenicity Analysis Set (IGS)

The Immunogenicity Analysis Set (IGS) contains all the Anti-Drug Antibody and/or Neutralizing Antibody (ADA/NAb) evaluable patients, who are in the SAF analysis set with at least one ADA/NAb sample (with reportable results) taken pre-treatment (i.e., a baseline sample) and at least one ADA/NAb sample (with reportable result) taken post-treatment in the OLE period.

5.3. General Data Handling Rules and Presentation Specifications

The following general guidelines will apply to all statistical analyses and data presentations:

5.3.1. Analysis Period

5.3.1.1. On-Study Period

Unless otherwise specified, the efficacy analysis will be based on the on-study period, which is defined as from randomization to the day of last efficacy assessment for main study period prior to first study drug infusion in the OLE period for subjects who enrolled in the OLE period; or from randomization to the last day of any efficacy assessment for subjects who did not enroll in the OLE period.

For the safety analysis, all safety assessments beyond 60 days of last dose will be excluded from summary tables or figures.

5.3.1.2. On-Treatment Period

The on-treatment analysis includes only the assessments that are observed during On-Study Period as defined above (Section 5.3.1.1), or within 4 weeks after last study drug infusion in the main study period. On-treatment analysis as one of the sensitivity analyses will only be conducted for the primary efficacy endpoint.

5.3.2. Baseline and Change from Baseline Definitions

Baseline is defined as the last available value obtained prior to the first dose of study drug (or randomization date if no infusion received) if not specified otherwise (Section 5.5). The acceptable value on Day 1 will be used to define the baseline values. Unscheduled visits prior to the first dose will be considered for baseline.

Change from baseline will be calculated by subtracting the baseline value from the post-dose assessment for each subject.

5.3.3. Study Day Calculation

The day when a subject receives the first dose of study drug after randomization will be considered as Day 1 for all analysis.

Study day of an assessment/procedure is calculated as follows.

- For events on or after first dose:

  Study day = Event date – Day 1 date + 1.

- For events earlier than first dose:

  Study day = Event date – Day 1 date.

Note: Day 1 date will be the first dose date if the subject receives study treatment. Otherwise, it will be the randomization date if the subject does not receive the study treatment after randomization.

5.3.4. General Instructions on TFLs

- For continuous variables that are recorded as "<X" or ">X", the value of "X" will be used in the calculation of summary statistics.
- All percentages will be rounded to one decimal place. The percentage will be suppressed when the count is zero. All durations of time will have 1 decimal place.
- All tables and listings will have a header showing "FibroGen, Inc.", protocol number (study nickname), date of data cutoff, and Page x of y. A footer will show the program file path/name, date of data extraction, run date and run time.
- More details are available in Appendix 5.

5.3.5. Handling Dropouts and Missing Data

All assessments collected will be considered for analyses regardless of whether such data are collected during treatment or after a subject discontinued treatment. All analyses assume the missing data are missing at random (MAR) unless stated otherwise. Detailed missing data handling are described in the analysis of specific endpoints.

5.4. Interim Analysis and Data Monitoring Committee

In addition to routine safety monitoring, an independent DMC is established to review safety data on an ongoing basis. A DMC charter will establish the procedures, meeting frequency, and scope of responsibilities of the committee.

This study has no planned or pre-specified interim analysis for either efficacy or futility.

5.5. Analysis Visit Windows

In accordance with Food and Drug Administration (FDA)/ European Medicines Agency (EMA) Guidance: During the COVID-19 pandemic, the visit modality (e.g.: in-person versus remotely) and scheduling maybe adjusted and conducted at the discretion of the Investigator, in accordance with the site's rules and recommendations, and using all necessary precautions. If a visit must be done remotely, it can be conducted with any technology available to the site and study subjects, such as via tele-health visits, phone calls, etc.

Analysis visits, instead of the nominal visits from case report form (CRF), derived from visit dates and visit time windows will be used in the by-visit analyses. Unscheduled visits within a visit window (defined in Appendix 2) will be grouped into the closest scheduled visits based on the visit date. For subjects who have more than one measurement at a certain analysis visit, the last measurement will be used, with the following exceptions:

- Liver function tests, such as Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Gamma-Glutamyl transferase (GGT), Alkaline Phosphatase (ALP), and total bilirubin, in which the maximum value will be used.
- Vital signs: the values on the infusion days will be used if applicable.
- Spirometry data: the Best Test Read (BTR) values will be used for analysis.

Efficacy parameters will be summarized by analysis visit defined by the following assessment windows (Appendix 2). The date of the first dose will be considered as the date of Day 1 for all analyses. Subjects will receive study drug every 2 weeks. The visit window for these visits is ±3 days. Duchenne Video Assessment can be performed in the subject's home up to 14 days prior to the scheduled study visit.

6. STATISTICAL ANALYSES

6.1. Subject Enrollment and Disposition

6.1.1. Eligibility

Eligibility will be summarized for all screened subjects. The data will be summarized with respect to:

- number of subjects screened
- number (%) of subjects screen-failed
- number (%) of subjects for each failed inclusion/exclusion criterion

Subject level inclusion criteria not met/exclusion criteria met listings will be provided.

6.1.2. Subject Accountability and Disposition

The number (%) of subjects randomized (ITT), dosed (SAF), Per-Protocol Set (PPS), completed the main study, entered the OLE period, and discontinued prematurely from treatment and study in the main study and OLE respectively will be presented for each treatment group and for all subjects pooled.

Reasons for premature discontinuation of treatment in the main study will be summarized by treatment group for the ITT population. A listing for the subjects who discontinue treatment prematurely in the main study will be presented.

6.2. Important Protocol Deviations

Important protocol deviations of interest may include, but are not limited to, the following:

- Entry Deviation: Subjects who entered the study, but did not meet inclusion/exclusion criteria
- Withdrawal Deviation: Subject met withdrawal criteria during the study but was not withdrawn.
- Dosing Deviation: Subject received the wrong treatment or incorrect dose; including incorrect timing of a dose; or subjects who missed more than 10% doses of prescribed study medication during the overall treatment period.
- Prohibited Medication Deviation: Subject received disallowed concomitant medications or non-drug therapy.

All above protocol deviations will go through the medical review process.

A subset of pre-specified important protocol deviations will be defined as major protocol deviations and subjects with major protocol deviations will be excluded from PPS analysis.

The number and percentage of subjects with important protocol deviations will be categorized and tabulated as appropriate for the ITT population. COVID-19 related important protocol deviations will be summarized separately. All protocol deviations will be finalized prior to database lock and unblinding.

6.3. Demographics and Baseline Characteristics

Demographics and baseline characteristics will be summarized descriptively for subjects in ITT and SAF. Each parameter will be presented in data listings.

Baseline values for efficacy assessments will be presented in baseline tables as appropriate.

6.3.1. Demographics and Baseline Characteristics

Demographic parameters and other important baseline and disease characteristics will be summarized by treatment group. These include but may not be limited to age, ethnicity, race, weight, body-mass index (BMI), and body surface area (BSA), total score of NSAA.

Computation formula:

BSA = [Weight $^{0.425}$ (kg) * Height $^{0.725}$ (cm)] x 0.007184

Age = Year of informed consent date – Year of birth

Descriptive statistics (n, mean, standard deviation, median, interquartile (Q1, Q3), range (=minimum, maximum) will be presented for continuous variables. Frequency distributions (number and percentage of subjects) will be presented for categorical variables.

6.3.2. Baseline DMD Disease Characteristics

Baseline DMD disease characteristics include:

1. Age in years when DMD was diagnosed = Year of date of diagnosis - Year of birth
2. Age when subject initiated ventilation = Year of date when subject initiated ventilation - Year of birth

3. Years since subject initiated ventilation = Current age – Age when subject initiated ventilation
4. Corticosteroids use: yes or no. If yes, age when subject began corticosteroids (= Year of date of subject began corticosteroids - Year of birth), and years since subject began corticosteroids (= Current age – Age when subject began corticosteroids).
5. Spine surgery: yes or no. If yes, age when spine surgery (=Year of Date of subject began spine surgery - Year of birth) was done, and years since the most recent spine surgery (= YRDIF (Date of spine surgery, Day 1 Visit Date, 'Actual'))
6. Is exon 44 deleted? – yes or no

Additionally, the following baseline disease characteristics, but are not limited to, will be summarized.

7. Bone parameters
   - Bone fractures (Refer to Section 6.8.7)
   - Scoliosis
   - Osteoporosis
8. Joint contractures
9. Cardiac parameters
   - Cardiomyopathy
10. Respiratory parameters
    - Ventilation support
    - Number of years since ventilation support initiated
    - Sleep apnea
    - ppFVC
11. Metabolic parameters
    - Insulin resistance
    - Obesity
    - Vit D deficiency
    - Delayed puberty
12. Corticosteroids (CS) use
    - Age at CS initiation
    - Prednisone/Prednisolone
    - Deflazacort
    - Regimen

- Daily
- Other

Other symptoms such as headaches, attention deficit hyperactivity disorder (ADHD), and autism spectrum disorder will also be summarized.

6.3.3. Medical History

Medical History of interest including allergies and surgeries, coded in system organ class (SOC) and preferred term (PT) using MedDRA (version 25.0 or higher), will be summarized for the ITT Analysis Set. Subject medical history listings will be provided.

6.4. Prior and Concomitant Medications

The World Health Organization Drug Dictionary (WHODD) Version (WHO Drug March 1, 2020, or later version) will be used to classify prior and concomitant medications by therapeutic class and generic name based on Anatomical Therapeutic Chemical (ATC) code level 3.

Prior medication is defined as any medication taken and stopped prior to the first infusion of the study medication. Concomitant medication is defined as any medication used concomitantly with the study drug that were not stopped before the first infusion or used concomitantly after the first infusion, ending 60 days after the last treatment. Partially or incomplete missing prior/concomitant medication start or stop date will be imputed (Appendix 1).

Both prior and concomitant medication usage will be summarized by the number (%) of subjects receiving the drug within each therapeutic class and ATC code level 3 and preferred term for the SAF. Multiple usage of the same drug by a patient will be counted only once.

In addition, a listing of all medications (prior or concomitant) taken during the course of the study (from screening through the end of study) captured in Concomitant Medication CRF, as well as Non-Drug Therapies CRF will be provided. Separate reports are provided for the main and OLE studies respectively.

Data on concomitant DMD medications administered during the study are collected and analyzed accordingly. Summary of concomitant DMD medications such as types of corticosteroids and duration of corticosteroid will be provided.

To evaluate the use of co-administered medications that are narrow therapeutic CYP substrates, the clinical database of concomitant medication will be searched for presence of narrow therapeutic index cytochrome P450 substrates and summarized. The list of related medications will be finalized before database lock.

6.5. Study Drug Exposure and Treatment Compliance

6.5.1. Study Drug Exposure

The number and percentage of subjects who receive study medication will be summarized by treatment group for the SAF.

Duration of weekly exposure/treatment is calculated as:

Weeks in treatment = (last dose date - first dose date + 1)/7 (keep 1 decimal place).

Duration of weekly exposure will be tabulated by treatment group for the SAF analysis set.

The number of infusions and average infusion dose amount in mg and mg/kg, any interruption during infusion (Y/N), and reason for missed dose or interruption will be summarized for the SAF analysis set.

6.5.2. Treatment Compliance

Dosing for pamrevlumab (or placebo) will be based on subject's body weight, which will be measured at Screening and every 12 weeks thereafter to determine dose for the subsequent 12-week interval. The total dose of pamrevlumab (or placebo) is not to exceed 4.1g per infusion or to align with the protocol. Subjects weighing more than 117 kg will receive the maximum allowable dose of 4.1g.

Compliance will be calculated as total amount of dosage (mg) the subject received divided by the total amount of dosage (mg) the subject is scheduled to receive during the participation in treatment.

$$Compliance\ (\%) = \frac{\text{actual total dosage received (mg)}}{\text{total planned dosage (mg) while actively in treatment}} \times 100$$

Descriptive statistics for study medication compliance will be presented by treatment group for the SAF. Treatment compliance will be summarized as a continuous variable and as a categorical variable (<70%, 70% –<80%, 80% –<90%, and 90% - 100%, >100%).

6.6. Efficacy Analyses

The primary and secondary endpoints will be tested using a fixed sequence procedure to preserve the study-wide error rate of 5%. Under the sequential analysis, the primary and secondary efficacy endpoints will be tested in a predefined sequence according to the order listed in Table 1 each at the usual alpha= 0.05 level of statistical significance. The testing will cease when a failure occurs in the pre-determined sequential hypothesis testing and all p-values for the subsequent testing will be considered nominal.

All analyses for efficacy endpoints will be performed for the ITT analysis set during the On-Study period (Section 5.3.1.1), unless noted otherwise.

Table 1: Testing Sequence of Primary and Secondary Endpoints

Testing Sequence	Endpoint
1 (primary endpoint)	Change in the total score of North Star Ambulatory Assessment (NSAA) from baseline to Week 52
2	Change in 4-stair climb Velocity (4SCV) assessment from baseline to Week 52
3	Change in the 10-meter walk/run test from baseline to Week 52
4	Changes in Time to Stand (TTSTAND) from baseline to Week 52
5	Time to Loss of Ambulation (LoA) from baseline to Week 52
6	Proportions of subjects in 10-meter walk/run test at Week 52

6.6.1. Primary Endpoint Estimand and Analysis

The primary efficacy endpoint in this study is defined as Change from Baseline in the total score of NSAA at Week 52.

The NSAA consists of 17 activities, each scored as 0, 1, or 2. The sum of these 17 scores will be used to form a total score. If fewer than 15 of the 17 activities are performed, the total score with be considered missing. If from 15 to 16 activities are performed, the total score will be calculated by multiplying the sum of the scores in the x activities that were performed by 17/x. If an activity cannot be performed due to disease progression or loss of ambulation, a score of zero will be assigned.

The primary efficacy endpoint will be analyzed using ITT as the primary analysis set.

The hypothesis to be tested for the primary efficacy analysis is:

> **H_0**: Change from Baseline in the total score of NSAA at Week 52 for the pamrevlumab arm = Change from Baseline in the total score of NSAA at Week 52 for the placebo group
>
> Versus:
>
> **H_1**: Change from Baseline in the total score of NSAA at Week 52 for the pamrevlumab arm ≠ Change from Baseline in the total score of NSAA at Week 52 for the placebo group

H_0 will be tested at the two-sided alpha = 0.05 level of significance and will be rejected if the $p < 0.05$ from the test.

6.6.1.1. Primary Analysis Using Mixed Model for Repeated Measure (MMRM)

6.6.1.1.1. Estimand Strategy

The primary estimand is intended to provide a population level estimate of the treatment effect of the pamrevlumab on a continuous endpoint, regardless of participant compliance with the IP dosing. Treatment policy strategy will be implemented, which means all observed measurements after randomization will be used in the primary analysis.

6.6.1.1.2. Population of Interest

The ITT population includes all randomized subjects during the on-study period as defined in Section 5.3.1.1.

6.6.1.1.3. Intercurrent Event Handling

Treatment discontinuation (such as due to adverse event, lost to follow-up, withdrawal by subject, physician decision, protocol deviations, etc.): Missing data will be implicitly imputed under missing at random assumption.

Death: The worst postbaseline score of all patients in the ITT population would be used to impute all missing values due to death. Missing study day will be imputed as target day of the corresponding analysis visit.

6.6.1.1.4. Analysis Variable

Change from baseline in the total score of NSAA in the main study period, including scheduled, unscheduled, and available assessments after treatment discontinuation, up to the targeted week 52 during the On-Study period (Section 5.3.1.1), will be included in the analysis.

6.6.1.1.5. Population Summary for Treatment Comparison

Treatment difference of Least-square mean (LSMean) and SE at week 52 and corresponding 95% CI will be presented.

The change in the total score of NSAA, from baseline to Week 52 will be analyzed using a Mixed Model for Repeated Measure (MMRM) with treatment, visit, visit-by-treatment interaction, baseline total score of NSAA, age, and corticosteroids use at baseline with appropriate covariance matrix (see section below) for the within subject covariance over time.

Covariance Structure Strategy

The unstructured covariance structure for the within-patient errors in the model will be applied first. The by-treatment-group option is included to the covariance pattern to improve the model efficiency.

If the algorithm for unstructured covariance pattern does not converge, the following covariance structures will be tested in sequence until the model converges: heterogeneous Toeplitz, homogeneous Toeplitz, first-order autoregressive, compound symmetry, and variance component. The sandwich estimator will be used if there is convergence issue. If the model does not converge for all covariance structures listed above, some least significant factors or interaction terms ($p>0.05$) can be excluded from the model to achieve convergence. The revised model with fewer factors or interaction terms will be tested using the same sequence as specified above.

6.6.1.2. Sensitivity Analyses of the Primary Endpoint

6.6.1.2.1. MI ANCOVA

Multiple Imputation Analysis of Covariance model (MI ANCOVA) will be performed to evaluate the robustness of the primary analysis as a sensitivity analysis.

6.6.1.2.1.1. Estimand Strategy

Same as Section 6.6.1.1.1.

6.6.1.2.1.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.1.2.1.3. Intercurrent Event Handling

Under the MAR assumption, subjects who discontinued from the treatment early alive are assumed to have the same data pattern as subjects who remain in the study for the same treatment arm. Multiple imputation will be carried out to impute missing data for visits up to Week 52.

Death: same as Section 6.6.1.1.3.

6.6.1.2.1.4. Analysis Variable

Same as Section 6.6.1.1.4 (Missing value imputation rules are defined below).

6.6.1.2.1.5. Population Summary for Treatment Comparison

The combined treatment difference of LSMeans (and SE) and the corresponding 95% CI for the estimated change from baseline in total score of NSAA at Week 52 will be presented.

Analysis will be performed in 3 steps.

Step 1 - First, the intermittent missing NSAA data will be imputed for each treatment relying on non-missing data from all subjects within each treatment group using the Markov Chain Monte Carlo (MCMC) imputation model with baseline NSAA, and the available non-missing NSAA to generate a monotone missing data pattern that only has missing data at end for planned visits through Week 52. The reported (observed) value will be used for multiple imputation. Change from baseline values will be derived using the difference between the imputed or observed post-baseline values and baseline values.

Then, for each dataset above, missing data will be imputed to derive 200 imputed datasets with non-missing data.

Step 2 - The 200 multiple-imputation datasets with imputed and observed NSAA data at Week 52 will be analyzed separately for each imputation using the ANCOVA method. The ANCOVA model will contain terms for treatment, baseline NSAA measurements, covariates. The ANCOVA model will include the same covariates as in the primary analysis. The LSMean and corresponding SE for the change from baseline in total score of NSAA at Week 52 will be estimated.

Step 3 - The SAS PROC MIANALYZE will be used to derive the final estimates and test statistics summarizing the 200 analysis results.

6.6.1.2.2. Pattern Mixture Models under MNAR for Missing Data: Jump-to-Control Analysis

The goal of the following analyses is to address the possibility of data being missing not at random (MNAR).

6.6.1.2.2.1. Estimand Strategy

Same as Section 6.6.1.1.1.

6.6.1.2.2.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.1.2.2.3. Intercurrent Event Handling

Treatment discontinuation (such as due to AEs, lost to follow-up, withdrawal by subject, physician decision, protocol deviations, etc.): The missing data pattern for the pamrevlumab subjects after withdrawal from the study can be assumed to switch to the same data pattern as subjects on the placebo treatment. Subjects that discontinued from the placebo arm are assumed to have the same data pattern as placebo subjects that remain in the study. This is often called the jump-to-control approach.

Death: same as Section 6.6.1.1.3.

6.6.1.2.2.4. Analysis Variable

Change from baseline in the total score of NSAA at Week 52 (Missing value imputation rules are defined below).

6.6.1.2.2.5. Population summary for treatment comparison

Under the jump-to-control assumption, the analysis will be carried out in 3 steps.

Step 1 - the missing NSAA data will be imputed to derive 200 imputed datasets with non-missing data according to the jump-to-control data pattern.

Step 2 - The 200 multiple imputation datasets with imputed and observed data will be analyzed separately using the ANCOVA method separately as described in Section 6.6.1.2.1.5.

Step 3 - The SAS PROC MIANALYZE will be used to derive the final estimates and test statistics summarizing the 200 dataset results.

The combined treatment difference of LSMeans, corresponding SE and 95% CI for the estimated change from baseline in total score of NSAA at week 52 will be presented.

6.6.1.2.3. Pattern Mixture Models under MNAR for Missing Data: Delta-Adjusting (Tipping Point) Analysis

6.6.1.2.3.1. Estimand Strategy

Same as Section 6.6.1.1.1.

6.6.1.2.3.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.1.2.3.3. Intercurrent Event Handling

Treatment discontinuation (such as due to AEs, lost to follow-up, withdrawal by subject, physician decision, protocol deviations, etc.): An alternative assumption is that the missing data for the pamrevlumab treated subjects who discontinue early have a lower expected value than the pamrevlumab subjects remaining in the study, while subjects who discontinue from the placebo arm are assumed to have the same data pattern as placebo subjects remaining in the study. This is often called the delta-adjusting (or tipping point) approach.

Death: same as Section 6.6.1.1.3.

6.6.1.2.3.4. Analysis Variable

Change from baseline in the total score of NSAA assessments at Week 52 (Missing value imputation rules are defined below).

6.6.1.2.3.5. Population summary for treatment comparison

The integrated treatment difference of LSMeans, corresponding SE and 95% CI for the change from baseline in total score of NSAA at week 52 will be presented.

The multiple imputation analysis will be performed as follows.

Step 1 - the missing NSAA data will be imputed to derive 200 imputed datasets with non-missing data according to the delta-adjusting data approach.

Step 2- The observed and imputed NSAA data will be analyzed using the ANCOVA method separately as described in Section 6.6.1.2.1.5 for each of the 200 imputed datasets. The LSMean and corresponding SE for the change from baseline in NSAA at week 52 will be estimated. Same as Step 2 in Section 6.6.1.2.1.5.

Step 3- The SAS PROC MIANALYZE will be used to summarize the final estimates and test statistics from the 200 dataset results. Same as Step 3 in Section 6.6.1.2.1.5.

6.6.1.2.4. On-treatment Analysis for Primary Efficacy Endpoint

A sensitivity analysis will be performed for NSAA assessed during on-treatment period as defined in Section 5.3.1.2.

6.6.1.2.4.1. Estimand Strategy

Same as Section 6.6.1.1.1.

6.6.1.2.4.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.1.2.4.3. Intercurrent Event Handling

Same as Section 6.6.1.1.3

6.6.1.2.4.4. Analysis Variable

Only on-treatment NSAA assessments will be included in the analysis

6.6.1.2.4.5. Population Summary for Treatment Comparison

Same as Section 6.6.1.1.5.

6.6.1.2.5. Cumulative Loss of Function Analysis for Primary Efficacy Endpoint

This sensitivity analysis used data representing cumulative failure to perform 17 items of NSAA in patients at multiple time points over 52 weeks.

6.6.1.2.5.1. Estimand Strategy

Failure to perform an item was defined as a score transition from 2 or 1 to 0 at evaluation. Only post-baseline failures were considered in the present analysis. For each treatment group, the mean of all such patients' individual curves will be constructed, reflecting the average cumulative number of failures over time. The higher the curve, the worse the study treatment effect. To quantify the group difference, we assume that the ratio of two corresponding underlying group-wise curves is constant over time, and use the Lin, Wei, Yang and Ying (LWYY) analytic method, which is the same as the Anderson-Gill method with the robust variance estimate, to estimate this constant ratio. This summary measure can also be interpreted as the ratio of the intensities of occurrences of failures over time. If this assumption is not plausible, the resulting estimate reflects an averaged ratio between the two curves over time. The lower the ratio, the greater the treatment effect.

6.6.1.2.5.2. Population of Interest

ITT as defined in Section 5.2.1.

6.6.1.2.5.3. Intercurrent Event Handling Strategy

If a patient discontinued, the cumulative failure number was censored upon discontinuation.

6.6.1.2.5.4. Analysis Variable

Cumulative counts of failure to perform 17 items of NSAA.

6.6.1.2.5.5. Population Summary for Treatment Comparison

All post-baseline visits during the double-blind period will be included in the analysis. Cumulative counts of failure to perform 17 items of NSAA at post-baseline visits will be analyzed using the Anderson-Gill method with the model-based covariance estimate to estimate

the ratio between treatment arms. Rate ratio between 2 arms including 95% CI and p-value will be reported. Sample SAS code is provided below.

```
proc phreg data=final covs(aggregate);
   model (TStart, TStop) * Status(1) = Trt Number;
   id id;
   where TStart < TStop;
run;
```

Note: 1= censored. For more information, please refer to SAS online help.

6.6.2. Secondary Endpoints Estimands and Analyses

The secondary endpoints during the on-study period (as defined in Section 5.3.1.1) will be analyzed in the order specified in Table 1.

6.6.2.1. Secondary Endpoints using MMRM Model

6.6.2.1.1. Estimand Strategy

Same as Section 6.6.1.1.1.

6.6.2.1.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.2.1.3. Intercurrent Event Handling

Same as Section 6.6.1.1.3.

6.6.2.1.4. Analysis Variables

6.6.2.1.4.1. Change in 4-Stair Climb Velocity (4SCV) assessment from baseline to Week 52

4SCV is calculated as the ratio of the number of stairs climbed divided by the number of seconds taken to complete the 4-stair climb. The result is converted into velocity (distance/time).

6.6.2.1.4.2. Change in the 10-Meter Walk/Run test from baseline to Week 52

The time required for a participant to run or walk a distance of 10 meters as quickly as possible is calculated as velocity (distance/time).

6.6.2.1.4.3. Changes in Time to Stand (TTSTAND) from baseline to Week 52

The time required for a participant to stand from supine position. A longer time reflects a worse outcome. A negative change from baseline indicates an improvement.

6.6.2.1.5. Population Summary for Treatment Comparison

Same as Section 6.6.1.1.5.

6.6.2.2. Time-to-Event Secondary Endpoints

6.6.2.2.1. Estimand Strategy

The secondary estimands are intended to provide a population level estimate of the treatment effect of the pamrevlumab on time-to-event endpoints, regardless of participant compliance with the IP dosing.

6.6.2.2.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.2.2.3. Intercurrent Event Handling

Treatment discontinuation (such as early termination due to AEs, Lost to Follow-Up, Withdrawal by Subject, Physician Decision, Protocol Deviations, etc.): treatment policy strategy will be employed, which means all observed data will be used regardless of treatment discontinuation.

Death: same as Section 6.6.1.1.3.

6.6.2.2.4. Analysis Variables

Time (Days) to Loss of Ambulation (LoA) is defined as the number of days from randomization to the date of loss of ambulation, or all-cause death based on observed data, whichever occurs earlier during the on-study period as described in Section 5.3.1.1.

Subjects without an event will be censored on the date of the last Muscle Function Tests (MFTs) assessment within 357 days after randomization, but prior to the first study drug infusion in the OLE period (for subjects who enrolled in the OLE period). Alive subjects who do not have any post-baseline MFT assessments will be censored on Day 1. Subjects who died after Week 10, but do not have any post-baseline MFT assessments will be censored on Day 1 as well. However, subjects who died within 10 weeks will be considered as an event.

6.6.2.2.5. Population summary for treatment comparison

The hazard ratio, corresponding SE, and 95% CI for the hazard ratio will be presented.

The Cox proportional hazard model by treatment will be used to estimate the hazard ratio and its corresponding 95% CI. A log-rank test by will be used for treatment comparison.

The number of subjects with Time to LoA will be summarized descriptively using the Kaplan-Meier method.

6.6.2.3. Proportions of subjects in 10-meter walk/run test at Week 52

6.6.2.3.1. Estimand Strategy

The estimand is to estimate the treatment effect of the pamrevlumab by comparing the proportions of subjects having results >10 seconds in 10-meter walk/run test at Week 52, regardless of participant compliance with the IP dosing.

6.6.2.3.2. Population of Interest

Same as Section 6.6.1.1.2.

6.6.2.3.3. Intercurrent Event Handling

Treatment discontinuation (such as early termination due to AEs, Lost to Follow-Up, Withdrawal by Subject, Physician Decision, Protocol Deviations, etc.): treatment policy strategy will be employed, which means all observed data will be used regardless of treatment discontinuation.

Death: same as Section 6.6.1.1.3.

6.6.2.3.4. Analysis Variables

Proportions of subjects having results in 10-meter walk/run test at Week 52.

6.6.2.3.5. Population summary for treatment comparison

The proportions of subjects having results >10 seconds or <=10 seconds in 10-meter walk/run test at Week 52 will be summarized and presented. Fisher's exact test will be used for treatment comparison of proportions of subjects having results >10 seconds. Two-sided P-value at significance level of 0.05 from Fisher's exact test is presented.

6.6.3. Exploratory Endpoint Analyses

6.6.3.1. Change in Duchenne Video Assessment severity percentage from baseline to Week 52

The DVA tool provides a standardized way to document and assess patient quality of movement. Caregivers will video record subjects doing specific movement tasks at home using a secure mobile application within 2 weeks prior to the clinic visits specified in the Schedule of Assessments. Trained physical therapists will score the videos in a secure scoring dashboard using scorecards with pre-specified compensatory movement criteria. Casimir, the organization that developed the DVA, will manage DVA data collection, quality, and scoring.

Summary of the listings and analyses Duchenne Video Assessment severity percentage and Clinical Global Impression of Change (CGI-C) scores will be based on the ITT population.

Details of DVA data analysis can be found in a separate document named "Duchenne Video Assessment Statistical Analysis Plan".

6.6.3.2. Change in ppFVC and ppPEF from Baseline to Week 52

Exploratory endpoints, the change from baseline to Week 52 in ppFVC and ppPEF will be analyzed using the same intercurrent handling and analysis method as for the primary endpoint.

6.6.3.3. Change in lower extremities vastus lateralis muscle fibrosis score from baseline to Week 52, assessed by MRI

Exploratory endpoint, the change from baseline at week 52 in fibrosis score of lower extremities, vastus lateralis muscle will be analyzed using an ANCOVA model, which contains terms for treatment, baseline measurements.

6.6.4. Subgroup Analyses of the Specified Endpoints

The subgroups may include but are not limited to:

- Age group (<= 9 years, > 9 years)
- Race (White, Other)
- Baseline total score of NSAA (<= median, > median)
- Corticosteroids use (Deflazacort, Prednisone/Prednisolone)
- Time to rise from the floor subgroup (<= 5, > 5 seconds)
- Baseline 10-meter walk/run Test subgroup (<= 5, > 5 seconds)
- ADA status (Positive, Negative)
- Regional subgroups:
    - US, Non-US
    - China, Non-China

The primary endpoint NSAA will be repeated for relevant and appropriate subgroups. Secondary endpoints 4SCV, 10-meter walk/run test, and TTSTAND will also be analyzed by subgroups. The LSMean of treatment difference and corresponding 95% CI will be presented in a forest plot as appropriate.

If the subjects who took the prohibited medications constitute to more than 10% of the population, then the subgroup analysis – with or without prohibited medications will be performed.

6.7. PK Analyses

A summary of drug concentrations by visit as well as a listing will be provided. A population PK analysis, as well as an exposure-response analysis, will be defined in a separate PK analysis plan.

6.8. Safety Analyses

6.8.1. Adverse Events

Adverse events will be coded using MedDRA version 25.0 or higher.

A new or worsening AE occurring on or after the first dose of study medication and within 60 days after the last dose of study drug is defined as a TEAE. Partially or incomplete missing AE start/stop date/time will be imputed (Appendix 1).

If more than one event occurs with the same SOC and PT for the same patient, the patient will be counted only once for that preferred term using the most severe and most related occurrence for the summarization by common terminology criteria for adverse events (CTCAE) severity grade and by relationship to the study medication. Relationship to study drug will be imputed as "Related" for any TEAE with missing value for relationship.

The following summary AE tables including number (%) of subjects will be produced:

- Summary of all TEAEs
- TEAEs by PT
- TEAEs by SOC and PT
- TEAEs by SOC, PT, and maximum severity
- TEAEs with severity grade ≥3 by SOC and PT
- TEAEs related to study medication determined by investigator by SOC and PT
- Common TEAEs (≥ 5% of subjects in either treatment arm) by SOC and PT
- Common non-serious TEAEs (≥ 5% of subjects in either treatment arm) by SOC and PT (Note: this is required for ClinicalTrials.gov)
- TEAEs leading to discontinuation of study medication by SOC and PT
- TEAEs leading to interruption of study medication by SOC and PT
- Treatment-emergent serious AEs (TESAEs) by SOC and PT
- TESAEs by SOC, PT, and maximum severity
- TESAEs related to study medication determined by investigator by SOC and PT
- Fatal TESAEs (i.e., adverse events that has an outcome of death) by SOC and PT
- All cause deaths

Listings of serious adverse events (SAEs), adverse events leading to study drug discontinuation, hypersensitivity, and infusion reactions, and all cause deaths will be provided.

Additionally, the following safety analyses will be conducted:

- Number and percentage subjects with bone fractures (Refer to Section 6.8.7)
- Number and percentage of subjects with hospitalizations due to any serious adverse events with pulmonary and/or cardiac cause(s), after the first dose of investigational product (IP)

Refer to Section 6.8.6 for special safety events such as hypersensitivity reactions and related topics.

6.8.2. Clinical Laboratory Assessments

Blood samples are drawn for the following analyses showed in Table 2 .

Table 2: Laboratory Tests

CBC:	**Chemistry Panel:**
Absolute neutrophil count (ANC)	BUN
Eosinophils	Creatine Kinase
RBCs (Erythrocyte count)	Creatinine
Hematocrit %	Chloride
Hemoglobin	Magnesium
WBCs (Leukocyte count)	ALP

Lymphocytes	ALT
Monocytes	AST
Neutrophils	Bilirubin, total
Platelets	Albumin
CRP	Phosphorous
Basophils	Potassium
	Sodium
	GGT
	Calcium
	GFR
	Cystatin-C

Laboratory test results and change from baseline are summarized by analysis visit and by treatment arm.

CTCAE grade 3 or higher lab test results will be considered potentially clinically significant (Appendix 4). These results are summarized and presented in a data listing.

Shift tables to summarize changes from baseline to each visit in CTCAE v5.0 categories are tabulated. Shift from baseline to most severe CTCAE category during the study is also summarized.

Due to central lab kit shortages caused by Covid-19, lab data may be collected using local labs in lieu of the central lab. The local lab data will be integrated with central lab data, when appropriate and feasible. Sensitivity analyses may be performed for key analyses of lab parameters with and without local lab values (i.e., set to missing).

An eDISH (evaluation of Drug Induce Severe Hepatotoxicity) analytical graph, which is a scatter plot of maximum observed total bilirubin versus maximum observed ALT or AST, will be generated to identify cases in Hy's law range.

6.8.3. Vital Signs

Pulse (beats/min), diastolic and systolic blood pressure (mmHg), respiration (breaths/min), and temperature (°C) will be descriptively summarized by treatment at selected visits.

Vital sign values are potentially clinically significant (PCS) if they meet both the observed value criteria and the change from baseline criteria listed in Table 3 below. The number and percentage of subjects with post-baseline PCS values will be tabulated by treatment group. The percentages are to be calculated relative to the number of subjects with baseline and at least one post-baseline assessment. The numerator is the total number of subjects with at least one post-baseline PCS vital sign value. A supportive listing of subjects with post-baseline PCS values will be provided including the treatment, subject ID, study center ID, baseline, and post-baseline values. A listing of all AEs for subjects with PCS vital signs will also be provided.

Table 3: Criteria for Potentially Clinically Significant Vital Signs

Vital Sign Parameter	Flag	Criteria*	
		Observed Value	Change from Baseline
Systolic Blood Pressure (mmHg)	High	≥170	Increase of ≥ 20
	Low	≤90	Decrease of ≥ 20
Diastolic Blood Pressure (mmHg)	High	≥110	Increase of ≥15
	Low	≤45	Decrease of ≥ 15
Pulse Rate (bpm)	High	≥120	Increase of ≥20
	Low	≤50	Decrease of ≥ 20
Weight (kg)	High	-	Increase of ≥20%
	Low	-	Decrease of ≥ 20%

* Except for body weight, a post-baseline value is considered as a PCS value if it meets both criteria for observed change from baseline.

6.8.4. Physical Examination

Clinically significant changes in PE results from baseline will be summarized by treatment over visit. A shift table will be provided if appropriate. A listing of clinically significant changes in PE results from baseline will be provided.

6.8.5. Electrocardiogram

ECG results will be provided in a listing only.

6.8.6. Special Safety Events

Treatment-emergent special safety events including:

1. Hypersensitivity (any time)
2. Infusion reactions (on day of infusion or 1 day post any study drug infusion)
3. Anaphylactic reactions (on day of infusion or 1 day post any study drug infusion)

Items 1 and 2 include both hypersensitivity and angioedema events. Both items will be listed and summarized similarly to TEAEs:

- Events by event type, SOC, PT, and maximum severity,
- Events by event type, SOC, PT.

Items 3 uses a modified SMQ to retrieve events under anaphylactic reactions and will be listed and summarized by treatment and PT only.

The preferred term list for these special safety events will be finalized prior to database lock.

6.8.7. Bone Fractures

Bone fractures are summarized, but not limited to, by types of bone fractures, namely, long bone fractures and vertebral compression fractures.

Long bones fractures:

- Lower extremities: femur (thigh); tibia; fibula (leg), metatarsus, phalanges (foot). Joint fractures: hip, knee, ankle;
- Upper extremities: humerus (arm); radius; ulna (forearm); metacarpus, phalanges (hand, palm); Joint fractures: shoulder, elbow, wrist.

Vertebral compression fractures:

Spine compression fracture, vertebral compression fracture, spine fracture, or vertebral fracture indicate the same type of vertebral compression fractures. The level of compression fracture is indicated by vertebrae: C1–C7 (cervical spine); T1–T12 (thoracic spine); L1–L5 (lumbar spine); S1-S5 (sacrum, fused), coccyx (3-5, fused).

Other:

Hip bone fracture; foot fracture (other than long bones); hand fracture (other than long bones); other.

6.8.8. Subgroup Analyses of Safety Endpoints

The subgroup analysis will be conducted for the safety endpoints of TEAEs and TESAEs. The subgroups are specified in Section 6.6.4 , including age, race, corticosteroids use, regional subgroups and ADA status.

6.9. Biomarker Endpoint Analysis

A sample for Tryptase at time of immunogenic reaction will be collected. A listing will be provided for the data.

6.10. Immunogenicity Analysis

Analysis of immunogenicity data will be based on IGS. Analysis dataset and data listing will include all available Human Anti-Human Antibody (HAHA, ADA) samples. The following terms and definitions are implemented.

6.10.1. Terms and Definitions

6.10.1.1. Sample ADA Status:

- Baseline ADA-positive sample: ADA is detected in the last sample before initiation of treatment.
- Baseline ADA-negative sample: ADA is not detected in the last sample before initiation of treatment.
- **Treatment-emergent ADA-Positive**: Meets definition of treatment-induced or treatment-boosted ADA. After initiation of treatment,
  - **Treatment-induced ADA-Positive**: a post-treatment positive ADA is detected in a subject for whom pre-treatment ADA assessment is either negative or not assessable, or

  - **Treatment-boosted ADA-Positive**: pre-existing ADA were boosted to a higher-level following study treatment, i.e. pre-treatment positive ADA titer was boosted by at least 2 dilution steps (4-fold) following study treatment.
- ADA-negative sample: After initiation of treatment, ADA is not treatment-emergent ADA-positive.

Next, using the sample ADA status, subject ADA status is defined.

6.10.1.2. Subject ADA Status:

- Baseline ADA-positive subject: A subject with baseline ADA-positive sample.
- ADA-positive subject: An evaluable subject with at least one treatment-emergent ADA sample at any time during the study.
- Neutralizing-positive: At least one treatment-emergent ADA-positive sample with neutralizing antibodies detected (if available).
- ADA-negative subject: An evaluable patient without a treatment-emergent ADA sample during the study.

6.10.2. Statistical Analysis for Characterization of ADA Immune Response

6.10.2.1. Incidence of ADA

- Percentage of treatment-emergent ADA patients for the defined study period, where the denominator is the number of ADA evaluable patients in the respective treatment arm and/or subgroup.
- Number (%) of subjects will be reported for the following parameters based on evaluable subjects:
  - Baseline ADA-positive
  - ADA-positive (Treatment-induced, Treatment-boosted)
  - Neutralizing Positive (if available)
  - ADA-negative
- **ADA prevalence**: Percentage of treatment-emergent ADA patients at any given timepoint, where the denominator is the number of ADA evaluable patients in the respective treatment arm and/or subgroup at that time point.
- A listing of all ADA assessments will be provided.
- Additionally, a separate listing of ADA assessments for all neutralizing antibody (NAb)-positive subjects will be provided (if available).

6.10.2.2. ADA Titer Kinetics

All ADA-positive subjects will be included in the analysis.

- Summary statistics of subject-level ADA titers using the maximum titer value within an ADA positive subject will be presented for baseline ADA-negative subjects and baseline ADA positive subjects. The median, interquartile range, and range of the maximum titers will be reported. For ADA-positive subjects with baseline ADA-positive sample, the median and interquartile range of the fold increase from baseline in titer (ratio of maximum post-baseline titer to baseline titer) will also be reported. Graphical presentation of the summary data may be provided using boxplots, as appropriate.
- For sample-level ADA titers, boxplots of ADA titers at each assessment timepoint will be provided, as appropriate, to demonstrate whether the ADA levels tend to change over time during the treatment, along with ADA incidence at each assessment timepoint.
- Spider plots may be considered to show the trend of ADA titer over time for subjects with >/= 5 ADA results by splitting subjects into multiple spider plots (e.g., $\approx \leqslant 10$ per plot, approximately.

6.10.3. Clinical Implication of ADA Immune Response

6.10.3.1. PK

- Effect of ADA response on the drug exposure will be explored by examining the drug exposures in subjects with ADA-positive versus ADA-negative status using graphical plots or simple summary statistics of observed drug concentration levels by sampling time. Corresponding numerical values of geometric mean, arithmetic mean, and standard deviation for each of ADA-positive subjects and ADA-negative subjects will be displayed under the figures.
- A listing of drug concentration with immunogenicity assessment at each pre-specified time point will be provided. Time course of observed concentrations by study visit with identifiers for antibody response will be plotted for each subject separately.

6.10.3.2. Safety

- Effect of ADA response on safety will be explored by examining the frequency and type of AEs of interest, including (1) Total TEAEs, (2) Drug Hypersensitivity, and (3) Infusion Reactions. For each category of AEs, summary tables for incidence will be provided for each of the preferred terms and overall within a category by ADA status, if the number of ADA-positive subjects is of sufficient size (e.g., at least ≈10 subjects). Otherwise, individual subject's safety profile will be examined and described based on a listing.
- Listings of AEs will be provided. These listing will also indicate study day and study period of the positive responses.

6.10.3.3. Efficacy

- Primary efficacy endpoint will be presented by ADA status.

- Efficacy listings for all positive subjects (relative to baseline) will be provided. These listing will also indicate study day and study period of the positive responses.

7. CHANGES FROM PROTOCOL

- Randomization stratification factor (Exon deletion status = yes, no) was dropped from all analysis models due to the small sample size in one of the factor levels.
- Cumulative Loss of Function Analysis (Section 6.6.1.2.5) was added as sensitivity analysis for the primary efficacy endpoint.
- Proportions of subjects in 10-meter walk/run test at Week 52 was added as a secondary efficacy endpoint.
- The baseline for MFT assessments is defined as the last evaluable value prior to the first study drug infusion (or randomization date if no infusion is received). If the assessment at Day 1 is not evaluable, the assessment at the Screening visit will be used.

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9. APPENDICES

APPENDIX 1. HANDLING MISSING/INCOMPLETE DATES

A.1 Missing/Incomplete AE Onset Date

The following imputation rules apply to the case where the start date is incomplete (i.e., partially missing) for adverse events.

A.1.1 Missing start time

AEs with missing start times and which occur on a study-drug-dosing day will be considered as occurred after the study drug administration on that day, that is, it will be considered as TEAE. No imputation on other missing times.

A.1.2 Missing day and month

If the year is same as the year of first day on double-blind study medication, then the day and month of the start date of double-blind study medication will be assigned to the missing fields.

If the year is not the same as the year of first day on double-blind study medication, then January 1 will be assigned to the missing fields.

A.1.3 Missing month only

Treat day as missing and replace both month and day according to the above procedure.

A.1.4 Missing day only

If the month and year are same as the year and month of first day on double-blind study medication, then the start date of double-blind study medication will be assigned to the missing day.

If the month and year are not the same as the year and month of first day on double-blind study medication, then the first day of the month will be assigned to the missing day.

Table 4: Analysis Date Derivation Rules for Missing/Incomplete AE Onset Date

Reported Date	Date of First Drug Intake	Analysis Date (Derived)
--/MM/YYYY	DD/MM/YYYY	
--/02/2008	14/02/2008	14/02/2008*
--/02/2008	14/02/2007	01/02/2008
--/02/2008	14/02/2009	01/02/2008
--/--/YYYY	DD/MM/YYYY	
--/--/2008	14/02/2008	14/02/2008
--/--/2008	14/02/2007	01/01/2008
--/--/2008	14/02/2009	01/01/2008
DD/--/----		No imputation
--/MM/----		
--/--/----		

*Death date has to be taken into consideration when calculating this.

If the stop date is complete and the imputed start date as above is after the stop date, the start date will be imputed by the stop date.

A.2 Missing/Incomplete AE Stop Date

If needed, the following imputation rules apply to the case where the end date is incomplete (i.e., partially missing) for adverse events. Other partial end dates will not be imputed.

A.2.1 Missing day and month, or Missing month only

December 31 will be assigned to the missing fields.

A.2.2 Missing day only

The last day of the month will be assigned to the missing day.

Table 5: Analysis Date Derivation Rules for Missing/Incomplete AE Stop Date

Reported Date	Analysis Date (Derived) *
--/MM/YYYY	Set as last day of the month 31/MM/YYYY or
	30/MM/YYYY or
	29/MM/YYYY or
	28/MM/YYYY
--/--/YYYY	31/12/YYYY
DD/--/----	No imputation
--/MM/----	
--/--/----	

*Death date has to be taken into consideration when deriving this.

A.3 Missing/Incomplete Prior or Concomitant Medication Start Date

For prior or concomitant medications, incomplete (i.e., partially missing) start date is imputed the same way as for the AE described above. When the start date and the stop date are both incomplete for a patient, impute the start date first.

The following rules will be applied to impute the missing start date. If the stop date is complete and the imputed start date is after the stop date, then the start date will be imputed using the stop date.

A.3.1 Missing day and month

If the year of the incomplete start date is the same as the year of the first dose date of double-blind study medication, then the day and month of the first dose date will be assigned to the missing fields.

If the year of the incomplete start date is not the same as the first dose date of double-blind study medication, then January 1 will be assigned to the missing fields.

A.3.2 Missing month only

Treat day as missing and replace both month and day according to the above procedure.

A.3.3 Missing day only

If the month and year of the incomplete start date are the same as the month and year of the first dose date of double-blind study medication, then the day of the first dose date will be assigned to the missing day.

If the month and year of the incomplete start date are the same as the first dose date of double-blind study medication, then the first day of the month will be assigned to the missing day.

A.4 Missing/Incomplete Prior or Concomitant Medication Stop Date

The following rules will be applied to impute the missing stop date, if needed. If the last dose date of double-blind study medication is missing, impute it with the last visit date. If the imputed stop date is before the start date (imputed or non-imputed start date), then the imputed stop date will be replaced with the start date.

A.4.1 Missing day and month

If the year of the incomplete stop date is the same as the year of the last dose date of double-blind study medication, then the day and month of the last dose date will be assigned to the missing fields.

If the year of the incomplete stop date is not the same as the year of the last dose date of double-blind study medication, then December 31 will be assigned to the missing fields.

A.4.2 Missing month only

Treat day as missing and replace both month and day according to the above procedure.

A.4.3 Missing day only

If the month and year of the incomplete stop date are the same as the month and year of the last dose date of double-blind study medication, then the day of the last dose date will be assigned to the missing day.

If the month and year of the incomplete stop date are not the same as the month and year of the last dose date of double-blind study medication, then the last day of the month will be assigned to the missing day.

A.5 Missing Date Imputation for Last Dose Date

Imputed last dose date = earliest date of (last drug dispense date + number of days of drug dispensed, date of death, date of EOT/EOS visit, and other dates as appropriate).

APPENDIX 2. ANALYSIS VISIT WINDOWS

A.2. Analysis Windows

Analysis visits are defined by the windows that will have the widths of the corresponding assessments centered at the scheduled time. Unscheduled visits within a visit window defined below will be grouped into the closest scheduled visits based on the visit date.

Table 6: Analysis Visit Window for Vital Signs

Analysis Visit	Target Day	Start Day	End Day
Baseline	Last value before the first study drug infusion (or randomization date if no infusion received)		
Day 1 post-dose	1	1	1
Week 2	15	2	22
Week 4	29	23	36
Week 6	43	37	50
Week 8	57	51	64
Week 10	71	65	78
Week 12	85	79	92
Week 14	99	93	106
Week 16	113	107	120
Week 18	127	121	134
Week 20	141	135	148
Week 22	155	149	162
Week 24	169	163	176
Week 26	183	177	190
Week 28	197	191	204
Week 30	211	205	218
Week 32	225	219	232
Week 34	239	233	246
Week 36	253	247	260
Week 38	267	261	274
Week 40	281	275	288
Week 42	295	289	302
Week 44	309	303	316
Week 46	323	317	330
Week 48	337	331	344
Week 50	351	345	358
Week 52	365	359	**

** before the first study drug infusion in the OLE period or end of randomization treatment period
Note: The data on a study day with infusions will be used as a priority for summary tables whenever possible.
Note: All assessments beyond 60 days post last infusion will be excluded from summary tables or figures.

Table 7: Analysis Visit Window for Physical Examination

Analysis Visit	Target Day	Start Day	End Day
Baseline	Last value before the first study drug infusion (or randomization date if no infusion received)		
Week 12	85	2	127
Week 24	169	128	211
Week 36	253	212	309
Week 52	365	310	**

** before the first study drug infusion in the OLE period or end of randomization treatment period
Note: All assessments beyond 60 days post last infusion will be excluded from summary tables for labs.

Table 8: Analysis Visit Window for Pulmonary Function Tests (PFT)

Analysis Visit	Target Day	Start Day	End Day
Baseline	Last value before the first study drug infusion (or randomization date if no infusion received)		
Week 12	85	2	120
Week 22	155	121	190
Week 32	225	191	260
Week 42	295	261	330
Week 52	365	331	**

** before the first study drug infusion in the OLE period or end of randomization treatment period
Note: All assessments beyond 60 days post last infusion will be excluded from summary tables for labs.

Table 9: Analysis Visit Window for Muscle Function Tests (MFT)

Analysis Visit	Target Day	Start Day	End Day
Baseline*	Last value before the first study drug infusion (or randomization date if no infusion received)		
Week 10	71	2	106
Week 20	141	107	176
Week 30	211	177	246
Week 40	281	247	323
Week 52	365	324	**

* Please refer to the Section 7 for details
** Before the first study drug infusion in the OLE period or end of randomization treatment period
Note: All assessments beyond 60 days post last infusion will be excluded from summary tables for labs.

Table 10: Analysis Visit Window for Laboratory Tests

Analysis Visit	Target Day	Start Day	End Day
Baseline	Last value before the first study drug infusion (or randomization date if no infusion received)		
Week 8	57	2	85
Week 16	113	86	141
Week 24	169	142	197
Week 32	225	198	253
Week 40	281	254	309
Week 48	337	310	365
Week 56	393	366	**

** before the first study drug infusion in the OLE period or end of randomization treatment period
Note: All assessments beyond 60 days post last infusion will be excluded from summary tables for labs.

Table 11: Analysis Visit Window for Immunogenicity Data

Analysis Visit	Target Day	Start Day	End Day
Baseline	Last value before the first study drug infusion (or randomization date if no infusion received)		
Week 24	169	2	197
Week 32	225	198	253
Week 40	281	254	309
Week 48	337	310	**

** before the first study drug infusion in the OLE period or end of randomization treatment period

APPENDIX 3. NORTH STAR AMBULATORY ASSESSMENT (NSAA)

The North Star Ambulatory Assessment (NSAA) worksheet should be used to document the scores for the assessments. A separate manual will be provided as a guide on how the tests should be conducted.
Note: The Time to Stand (from Supine) test is called Rise from Floor and is contained within the NSAA.

Activity	2	1	0	Score
1. Stand *3	Stands upright, still, symmetrical, without compensation (heels flat and hips in neutral rotation) for minimum count of 3 seconds	Stands still but with compensation (e.g. on toes or with legs abducted or with bottom stuck out/hip flexion, etc.) for minimum count of 3 seconds	Cannot stand still or cannot stand independently, needs support (even minimal)	
2. Walk *3	Walks consistently with heel-toe or flat-footed gait pattern	Persistent or habitual toe walker, unable to heel-toe consistently	Loss of independent ambulation – may use knee-ankle-foot orthosis (KAFO) or walk short distances with assistance	
3. Stand up from chair *3	Able to stand up keeping arms folded	With help from thighs / push on chair / prone turn or alters starting position by widening base (moving feet apart)	Unable	
4. Stand on one leg – right *3.5	Able to stand upright in a relaxed manner (no fixation) for a count of 3 seconds	Stands but either momentarily or with trunk side-flexion (20◦) or needs fixation e.g. by thighs adducted	Unable	
5. Stand on one leg – left *3.5	Able to stand upright in a relaxed manner (no fixation) for a count of 3 seconds	Stands but either momentarily or with trunk side-flexion (20◦) or needs fixation e.g. by thighs adducted	Unable	
6. Climb box step – right *3	Faces step – no support needed	Goes up sideways / rotates trunk / circumducts hip / needs hands for balance or hands on legs	Unable to perform independently	
7. Descend box step – right *3.5	Faces forward, steps down controlling weight-bearing leg. No support needed	Sideways / skips down / needs hands for balance or hands on legs	Unable without more than minimal support, or requires hands for support	
8. Climb box step – left *3	Faces step – no support needed	Goes up sideways / rotates trunk / circumducts hip / needs hands for balance or hands on legs	Unable to perform independently	
9. Descend box step -left *3.5	Faces forward, steps down controlling weight-bearing leg. No support needed	Sideways / skips down / needs hands for balance or hands on legs	Unable without more than minimal support, or requires hands for support	
10. Lifts head *4	In supine, full neck flexion, head must be lifted in mid-line. Chin moves towards chest	Head is lifted through side flexion, partial neck flexion, or with protraction	Unable. No clearance of head from surface	
11. Gets to sitting *3	Starts in supine – may use one hand / arm to push up	Uses two arms / pulls on legs or turns towards floor or uses momentum/rocking	Unable	

12. Rise from floor *4	No evidence of Gower's maneuver	Exhibits at least one of the components described above – in particular rolls towards floor, and/or use hand(s) on legs	(a) NEEDS to use external support object e.g. chair, wall OR (b) Unable NO TIME RECORDED	
13. Stands on heels *3.5	Both feet at the same time, clearly standing on heels only (acceptable to move a few steps to keep balance) for count of 3	Raises forefoot on both feet – all metatarsal heads off ground – or clearly dorsiflexes one foot only	Unable	
14. Jump *3	Both feet at the same time, clear the ground simultaneously and land at the same time	One foot after the other (skip) or does not fully clear both feet at the same time	Unable	
15. Hop right leg *4	Entire foot clears the floor	Able to bend knee AND raise heel, no floor clearance	Unable or only raises heel	
16. Hop left leg *4	Entire foot clears the floor	Able to bend knee AND raise heel, no floor clearance	Unable or only raises heel	
17. Walk Run (10 m) *3	Both feet off the ground (no double stance phase during running)	'Duchenne jog' or fast walk	Walk	
			TOTAL=	**/34**

Timed RFF: no time if uses furniture _____.____ **Timed 10m run / walk** _____.____

Age at which 85% of controls achieve full score *3 = 3 years of age, *3.5 = 3.5 years of age, *4 = 4 years of age (Mercuri 2016)

APPENDIX 4. LABORATORY TEST CTCAE CRITERIA

The following table is extracted from NCI Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0

Chemistry

		Grade 1	Grade 2	Grade 3	Grade 4
Bicarbonate	Decreased	<LLN and no intervention initiated	None	None	None
Creatinine		ULN – 1.5 x ULN	>1.5 – 3.0 x baseline[2] >1.5 – 3.0 x ULN	>3.0 x baseline[2] >3.0 – 6.0 x ULN	>6.0 x ULN
Albumin	Decreased	3 g/dL – LLN	2 - <3 g/dL	<2 g/dL	
Alkaline phosphatase (ALP)		ULN – 2.5 x ULN[4]; 2.0 - 2.5 x baseline[5]	>2.5 – 5.0 x ULN[4]; >2.5 - 5.0 x baseline[5]	>5.0 – 20.0 x ULN[4]; >5.0 - 20.0 x baseline[5]	> 20.0 x ULN[4]; >20.0 x baseline[5]
ALT		ULN – 3.0 x ULN[4]; 1.5 - 3.0 x baseline[5]	>3.0 – 5.0 x ULN[4]; >3.0 - 5.0 x baseline[5]	>5.0 – 20.0 x ULN[4]; >5.0 - 20.0 x baseline[5]	>20.0 x ULN[4]; >20.0 x baseline[5]
AST		ULN – 3.0 x ULN[4]; 1.5 - 3.0 x baseline[5]	>3.0 – 5.0 x ULN[4]; >3.0 - 5.0 x baseline[5]	>5.0 – 20.0 x ULN[4]; >5.0 - 20.0 x baseline[5]	>20.0 x ULN[4]; >20.0 x baseline[5]
Total bilirubin		ULN – 1.5 x ULN[4]; > 1.0 - 1.5 x baseline[5]	>1.5 – 3.0 x ULN[4]; >1.5 - 3.0 x baseline[5]	>3.0 – 10.0 x ULN[4]; >3.0 - 10.0 x baseline[5]	>10.0 x ULN[4]; >10.0 x baseline[5]
Calcium (Corrected)	Decreased	8.0 mg/dL – LLN	7.0 - <8.0 mg/dL	6.0 - <7.0 mg/dL	<6.0 mg/dL
		ULN – 11.5 mg/dL	>11.5 – 12.5 mg/dL	>12.5 – 13.5 mg/dL	>13.5 mg/dL
Glucose (Random)	Decreased	55 mg/dL – LLN	40 - <55 mg/dL	30 - <40 mg/dL	<30 mg/dL
Potassium	Decreased	3.0 mmol/L – LLN	3.0 mmol/L – LLN[1]	2.5 - <3.0 mmol/L	<2.5 mmol/L
		ULN – 5.5 mmol/L	>5.5 – 6.0 mmol/L[3]	>6.0 – 7.0 mmol/L	>7.0 mmol/L
Sodium	Decreased	130 mmol/L – LLN	125-129 mmol/L and asymptomatic	125-129 mmol/L symptomatic; 120-124 mmol/L regardless of symptoms	<120 mmol/L
		ULN – 150 mmol/L	>150 – 155 mmol/L[3]	>155 – 160 mmol/L	>160 mmol/L
Magnesium	Decreased	1.2 mg/dL – LLN	0.9 - <1.2 mg/dL	0.7 - <0.9 mg/dL	<0.7 mg/dL

		ULN – 3.0 mg/dL	None	>3.0 – 8.0 mg/dL	>8.0 mg/dL

Serum Hematology

		Grade 1	Grade 2	Grade 3	Grade 4
Hemoglobin	Decreased	10.0 g/dL – LLN	8.0 - <10.0 g/dL	<8.0 g/dL	
		>0 – 2 g/dL	>2 – 4 g/dL	>4 g/dL	
Platelet	Decreased	75,000 /mm^3 – LLN	50,000 – <75,000 /mm^3	25,000 - <50,000 /mm^3	<25,000 /mm^3
WBC	Decreased	3,000 /mm^3 – LLN	2,000 - <3,000 /mm^3	1,000 - <2,000 /mm^3	<1,000 /mm^3
		None	None	>100,000 /mm^3	
aPTT		ULN – 1.5 x ULN	>1.5 – 2.5 x ULN	>2.5 x ULN	
Lymphocytes	Decreased	800 /mm3 – LLN	500 - <800 /mm^3	200 - <500 /mm^3	<200 /mm^3
		None	>4,000 – 20,000 /mm^3	>20,000 /mm^3	
Neutrophils	Decreased	1500 /mm3 - LLN	1000 - <1500 /mm3	500 - <1000/mm3	<500/mm3
Eosinophils		>ULN and >Baseline	None	Steroids initiated	None

Decreased: below LLN; Otherwise, above ULN;
[1] Symptomatic, Intervention indicated
[2] Baseline is used if it is above ULN
[3] Intervention indicated
[4] ULN is used if Baseline was normal
[5] Baseline is used if Baseline was abnormal

APPENDIX 5. GENERAL SPECIFICATIONS FOR TABLES, LISTINGS, FIGURES

1. Software Used

All programming of tables, listings and figures (TFLs) will be performed using the statistical software package SAS® version 9.4 or greater.

2. General

All TFLs are based on Study Data Tabulation Model (SDTM) and/or Analysis Data Model (ADaM) datasets. By default, data listings reflect the actual values captured in SDTM and ADaM datasets, including date/time variables and missing values. Except for concatenation of some variables for compact display purpose, data are presented directly with minimum manipulation. In general, the character standard result variables is presented in data listings.

For continuous variables that are recorded as "<X" or ">X", the value of "X" will be used in the calculation of summary statistics. The value "X" is also captured in the numeric variable in the SDTM datasets as well as in the ADaM datasets for consistency, although SDTMIG recommends capturing missing values in the numeric variables.

3. Page Layout

All column headers (consisting of one or several words) will start with uppercase and thereafter only lowercase characters, except for acronyms and abbreviations. In case values from the database will be displayed in column headers, they may be displayed as in the database. Pages will be numbered as 'Page x of y', where 'y' is the total number of pages of the corresponding table or listing. The page specifications are presented in Table 3.

Table 12: Specifications for Page Layout

Paper Size	Letter
Orientation	Landscape
Alignment	Center
Font size	9
Font type	Courier New (default)
Margins:	
Top	1.0"
Bottom	0.4"
Left	1.0"
Right	0.4"

The margin sizes and font size for listings may be flexible to provide sufficient information on a single page to facilitate review and comparison.
When created using SAS, tables and listings will be created using ODS, and output files will be produced in RTF. When RTF files are produced, titles and footnotes will appear as document headers/footers.

4. Titles and Footnotes

All tables and listings will have a header showing “FibroGen, Inc.”, the protocol number, database cutoff date or ‘Final Database’, and Page x of y. A footer will show the program file path/name, output file path/name, run date and time.

All titles are written in title format, with uppercase at the beginning of each word; articles, prepositions, and conjunctions, which are of three characters length or less will start with lowercase letters (Mixed Case). Footnotes are in regular text format.

Titles

In total there are up to 10 titles available, defined as following:

first title “FibroGen, Inc.” (left aligned) and “Date of Data Cutoff : ddMMMyyy” (right aligned)

second title protocol number “Protocol: FGCL-3019-093 (LELANTOS(NA))” (left aligned) and “Page x of y” (right aligned)

third title blank

fourth title: table/listing/figure number

fifth title: table/listing/figure title

sixth title: population names if provided in SAP, or brief definition of specific analysis set

Footnotes

Up to 10 footnote lines are available for tables, listings and figures. Footnotes 1, 9 and 10 are standard. Footnotes 2 to 8 (left aligned) might be used as needed. They are to be specified in the Shell.

first footnote is a separating horizontal line.

second – eighth are free text which can be used for explanations. Footnotes will be referenced using numbers in square brackets, starting with [1], followed by [2] etc.

ninth footnote left blank; in case needed may also be used as for explanations.

tenth footnote the program name and the date of data extraction (left aligned); the date and time in the format ddMMMyyyy hh:mm when the output was created; the version (e.g. draft or final); and the word “Confidential”.

Footnotes are denoted by [1], [2], and so on.

5. Table, Figure, Listing Metadata

The table, figure, and listing (TFL) metadata will include the TFL numbers, titles, analysis populations, program names, input dataset names. For tables and figures, PARAMCD, PARAM, and other conditions will be specified. TFL numbers, titles, and footnotes will be imported from this master spreadsheet. In addition, this spreadsheet will record the names of the original programmer and the validator/reviewer and the date of validation approval.

6. Significant Digits of Summary Statistics

All percentages will be rounded to one decimal place and lined up by the decimal place. The percentage will be suppressed when the count is zero.

Any p-values will be rounded to four decimal places and will be presented as '<.0001' if they are less than 0.0001 after rounding.

For variables of direct measurements, summary statistics are displayed with the following specifications of decimal places in Table 13.

Table 13: Significant Digits of Summary Statistics

Description	Characteristic	Number of decimal places
Count	N	0
Mean	Mean	As in source + 1
Standard deviation	SD	As in source + 2
Standard error of the mean	SE	As in source + 2
Confidence Interval	CI	As in source + 1
Minimum	Min	As in source
Median	Median	As in source + 1
Maximum	Max	As in source
Q1 / Q3	Q1/Q3	As in source + 1
Percentage	%	All percentages will be rounded to one decimal place and lined up by the decimal place. The percentage will be suppressed when the count is zero
Coefficient of variation	CV (%)	1
p-value	p-value	p-values will be rounded to four decimal places and will be presented as '<.0001' if they are less than 0.0001 after rounding

N=number; Std=Standard deviation; CI=Confidence Interval; Min=minimum; Max=maximum; CV=Coefficient of variation

As a general guideline for derived parameters, three significant digits may be displayed for a parameter with an overall mean less than 100; otherwise, one decimal place may be used. If a derived parameter is in the same scale as some related measured parameters, such as MAP, QTc, the same display format may be used as the measured parameters.

Summary Statistics are to be displayed in the following order: Count, Mean, Standard Deviation, <Coefficient of Variation, Standard Error of the Mean, Confidence Interval>, Minimum, <Q1>, Median, <Q3>, Maximum.

For categorical variables the categories will be displayed in the TFLs in the same order they appear in the CRF.

7. Figure Specifications

In general, figures should include annotation of key summary statistics: n, mean, SE, median for continuous variables; n and percent for categorical variables; number of subjects at risk and

cumulative number of events as well as median and 95% CI for time-to-event data. Other statistics such as quartiles, ranges may be included depending on need and space.

P-values should be presented if comparisons are of interest.

For scatter plots, linear or non-linear trend lines should be included if the association of the two variables is of interest. Correlation coefficient or regression coefficients as well as corresponding p-values should be presented.

For box plots, 'BOXSTYLE=SCHEMATIC' should be used. The whiskers are drawn to the most extreme points in the group that lie within the fences. The upper fence is defined as the third quartile (represented by the upper edge of the box) plus 1.5 times the interquartile range. The lower fence is defined as the first quartile (represented by the lower edge of the box) minus 1.5 times the interquartile range. Observations outside the fences are identified with a special symbol.

APPENDIX 6. CHINA CDE REQUIREMENTS

Efficacy data, mainly including overseas key clinical trial data and clinical trial data conducted in China, should not only confirm the efficacy of the study drug as a whole, but also analyze the consistency between Chinese subgroups and the overall population.

The point estimate of treatment effect in China subgroup divided by its counterpart in the overall population will be used for assessing efficacy consistency.

Safety data, including all domestic and foreign data used for safety evaluation, should be analyzed not only for overall safety, but also for consistency between Chinese subgroup and overall population.

All TFLs in China may be provided per China regulatory requirements if regulatory submission in China is pursued.

Signature Page for VV-CLIN-013131 v2.0

Approval Task	[redacted] 14-Aug-2023 22:35:34 GMT+0000
Approval Task	[redacted] 14-Aug-2023 22:37:34 GMT+0000
Approval Task	[redacted] 14-Aug-2023 22:37:49 GMT+0000
Approval Task	[redacted] 15-Aug-2023 01:21:57 GMT+0000
Approval Task	[redacted] 15-Aug-2023 13:58:04 GMT+0000
Approval Task	[redacted] 15-Aug-2023 14:38:17 GMT+0000
Approval Task	[redacted] 15-Aug-2023 16:48:30 GMT+0000
Approval Task	[redacted] 15-Aug-2023 17:30:25 GMT+0000

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