Fulcrum Therapeutics

FIS-002-2019

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, 48-Week, Parallel-Group Study of the Efficacy and Safety of Losmapimod in Treating Subjects with Facioscapulohumeral Muscular Dystrophy (FSHD) with Open-Label Extension (OLE)

08Jan2024

Statistical Analysis Plan
(Open-Label Extension Period)

Version *4.0*

Prepared by:

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List of Abbreviations

AE	adverse event
AESI	adverse event of special interest
ATC	Anatomical Therapeutic Chemical
BID	twice daily
BLQ	below the limit of quantitation
BMI	body mass index
CI	confidence interval
COA	clinical outcome assessment
COVID-19	coronavirus disease 2019
CRF	case report form
ECG	electrocardiogram
FSHD	facioscapulohumeral muscular dystrophy
FSHD1	facioscapulohumeral muscular dystrophy type 1
FSHD-HI	FSHD Health Index
LMV	lean muscle volume
LS	least-squares
MedDRA	Medical Dictionary for Regulatory Activities
MFF	muscle fat fraction
MFI	muscle fat infiltration
MFM	Motor Function Measure
MRI	Magnetic Resonance Imaging
MSK	musculoskeletal
OLE	open-label extension
PGIC	Patient's Global Impression of Change
PO	orally
PT	preferred term
RWS	Reachable Workspace
RSA	relative surface area
SAE	serious adverse event
SAP	statistical analysis plan
SAS	Statistical Analysis Software
SD	standard deviation
SE	standard error
SOC	system organ class
TEAE	treatment-emergent adverse events
TUG	Timed Up and Go
WHODD	World Health Organization drug dictionary

1. Introduction

This statistical analysis plan (SAP) describes the analyses and data presentation for the Open-label extension (OLE) part of protocol FIS-002-2019 which is being conducted under the sponsorship of Fulcrum Therapeutics (Fulcrum) in accordance with applicable standard operating procedures. The efficacy analyses will be conducted at OLE visits with available subject data. Statistical analyses are being conducted under contract with [redacted], part of Thermo Fisher Scientific, in collaboration with Fulcrum.

The Clinical, Data Management, and Biostatistics departments at [redacted] will work diligently and collaboratively with Fulcrum to ensure that the data collected and analyzed for this study are of high quality. This will be accomplished in part by having thorough edit checks written, programmed, and updated as needed.

This SAP is based on the protocols version 4.0 (COVID-19 Pandemic Emergency Amendment) dated 10Apr2020 and version 5.0 dated 16Aug2022. This SAP contains definitions of analysis population, derived variables, and statistical methods for the analysis of the OLE and in some parts of this SAP, a combination of placebo-controlled treatment period and OLE analysis. A separate SAP was created for the placebo-controlled treatment period.

The OLE will evaluate the safety, tolerability, and efficacy of long-term dosing with losmapimod in treating subjects with Facioscapulohumeral Muscular Dystrophy type 1 (FSHD1).

The term study drug that is being used throughout this document refers to losmapimod and/or placebo.

2. Objectives for OLE

2.1. Primary Objectives

The primary objective of the OLE is to evaluate the safety and tolerability of long-term dosing of losmapimod in FSHD1 subjects, based on protocol versions 4.0 and 5.0.

2.2. Secondary Objectives

The secondary objectives of the OLE are as follows:

- To evaluate the changes from baseline in MFF, LMV, and MFI in FSHD1 subjects, as measured by MSK MRI, based on protocol version 4.0.
- To evaluate the plasma concentrations of losmapimod in FSHD1 subjects, based on protocol versions 4.0 and 5.0.

2.3. Exploratory Objectives

The exploratory objectives of the OLE, based on protocol version 4.0, are as follows:

- To evaluate the changes from baseline in the following COAs:
  - RWS with and without weights
  - Classic and FSHD TUG
  - Muscle strength by hand-held quantitative dynamometry
  - MFM Domain I
  - FSHD-HI
  - PGIC
- To evaluate the changes from baseline in inflammatory, immune, apoptotic, and other muscle disease transcripts in circulating proteins in plasma and serum.

3. Investigational Plan

3.1. Overall Study Design and Plan

Once subjects reach Week 48, they will have the option to roll over into the OLE, with all subjects receiving 15 mg PO losmapimod tablets BID. Subjects who wish to roll over into the OLE must complete all procedures from the Week 48 end of placebo-controlled treatment period/start of OLE visit.

Subjects will remain in the OLE until study drug approval or until the study is discontinued by the sponsor. All subjects who complete or discontinue from treatment will complete a safety follow-up visit 7 days (+/- 3 days) after the last dose of study drug.

During the OLE, subjects will attend clinic visits approximately every 12 weeks. Study drug (open-label losmapimod) will be administered BID and should be taken with food. The first dose of OLE drug will be the day after the Week 48 visit.

The OLE will evaluate the safety and tolerability of long-term dosing with losmapimod in treating subjects with FSHD1. The efficacy data will be collected until protocol version 5.0 is executed. The efficacy analysis will be conducted when available efficacy data are fully cleaned.

Prior to the COVID-19 pandemic, subjects who reached the Week 24 visit had the option to roll over into the OLE. Subjects who had already rolled over to the OLE prior to the COVID-19 pandemic will remain on open label treatment. Their next clinic visits will follow the assessments for the Week 36 and Week 48 visits in the placebo-controlled portion of the study as described in the COVID-19 Pandemic Emergency protocol version 4.0. The first dose of OLE drug for these subjects will be the day after the Week 24 visit.

3.2. Study Endpoints

3.2.1. Primary Endpoint

The primary endpoint of the OLE is the safety of long-term treatment of losmapimod based on AEs, clinical laboratory tests, ECGs, vital signs, and physical examination, based on protocol versions 4.0 and 5.0.

3.2.2. Secondary Endpoints

The secondary endpoints of the OLE are as follows:

- Changes from baseline in MFF, LMV, and MFI after long-term dosing (at every 12-week time point), based on protocol version 4.0
- Plasma concentrations of losmapimod after long-term dosing (at every 12-week time point), based on protocol versions 4.0 and 5.0

3.2.3. Exploratory Endpoints

The exploratory endpoints of the OLE, based on protocol version 4.0, are as follows:

- Changes from baseline in COAs after long-term dosing (at every 12-week time point):
    - RWS with and without weights
    - Classic and FSHD TUG
    - Muscle strength by hand-held quantitative dynamometry
    - MFM Domain I
    - FSHD-HI
    - PGIC
- Changes from baseline in inflammatory, immune, apoptotic, and other muscle disease transcripts in circulating proteins in plasma and serum after long-term dosing (at every 24-week time point)

3.3. Treatments

During the OLE, all subjects will receive 15 mg losmapimod BID open-label.

4. General Statistical Considerations

The following conventions will be used for all data presentations and analyses unless otherwise specified.

Appropriate descriptive statistics will be computed and displayed for both continuous and categorical variables. For continuous and quantitative variables, summaries will include n (number of subjects with non-missing data), mean, standard deviation (SD), standard error (SE), Q1 (first quartile), Q3 (third quartile), median, minimum, and maximum. Reporting conventions for descriptive statistics will follow the [redacted] Standard TLF Guidelines. For categorical variables, summaries will include the number and percentage of subjects who are in a particular category. Percentages will be computed based on the number of non-missing data points for patients in the applicable analysis set. Reporting of percentages will follow the [redacted] Standard TLF Guidelines.

A total column will be presented for demographics, baseline characteristics, protocol deviation and concomitant medication summaries.

All data will be listed by treatment sequence, subject ID, age, sex, race, analysis period, and visit date, if available. Data from both the placebo-controlled treatment period and OLE will all be included in a listing. Any repeat assessments or additional assessments, along with any unscheduled visits, will be presented in the listings. Sort order of data listings will be treatment sequence, subject ID, analysis period, and visit date, if available.

Statistical tests will be 2-sided, unless otherwise specified. P-values will be reported to 4 decimal places, with p-values less than 0.0001 reported as "<0.0001".

All analyses will be performed using Statistical Analysis Software (SAS®, release 9.4 or higher). A separate document as an appendix to this SAP will contain the tables, listings, and figures (shells).

4.1. Analysis Periods

For the purposes of efficacy and safety data analysis, and for reporting, two analysis periods for post baseline data are defined: placebo-controlled treatment period and OLE. The placebo-controlled treatment period encompasses data through Week 48 or Week 24 for subjects who prior to the COVID-19 pandemic had the option to roll over into the OLE at Week 24. The OLE encompasses all losmapimod data starting a day after the Week 48 visit or Week 24 visit for subjects who prior to the COVID-19 pandemic had the option to roll over into the OLE at Week 24. The duration of OLE is defined for each subject as the time after completion of the Week 48 or Week 24 for subjects who prior to the COVID-19

pandemic had the option to roll over into the OLE at Week 24 through completion of the safety follow-up after the end of treatment or discontinuation of the study.

In addition, a supplementary analysis period will be considered which is the losmapimod exposure period that encompasses all losmapimod exposure data, irrespective of when the losmapimod exposure starts (i.e., baseline or OLE).

4.2. Treatment

Data will be summarized according to sequence of treatment assignment and entry point of OLE:

- Placebo BID/Losmapimod 15 mg BID for subjects who completed 48 weeks of treatment in the placebo-controlled treatment period: This will include subjects who were assigned to Placebo at baseline and shifted to losmapimod 15 mg BID after Week 48 visit.
- Losmapimod 15 mg BID/Losmapimod 15 mg BID for subjects who completed 48 weeks of treatment in the placebo-controlled treatment period: This will include subjects who were assigned to losmapimod at baseline and shifted to losmapimod 15 mg BID after Week 48 visit.
- Placebo BID/Losmapimod 15 mg BID for subjects who completed 24 weeks of treatment in the placebo-controlled treatment period: This will include subjects who were assigned to Placebo at baseline and shifted to losmapimod 15 mg BID after Week 24 visit.
- Losmapimod 15 mg BID/Losmapimod 15 mg BID for subjects who completed 24 weeks of treatment in the placebo-controlled treatment period: This will include subjects who were assigned to losmapimod at baseline and shifted to losmapimod 15 mg BID after Week 24 visit.

4.3. Handling of Missing Data

All missing and partial dates for the concomitant medications and adverse events will be handled as outlined in Sections 7.1 and 9.1, respectively.

In categorical summaries, a missing category will be included if and only if any data for the given endpoint is missing.

Missing values for other individual data points will remain as missing, unless otherwise, stated.

4.4. Baseline, Study Day, and Change from Baseline Definitions

Unless indicated otherwise, baseline will be defined as the last non-missing evaluation on or before the day of first dose of study drug in the placebo-controlled treatment period. If the last non-missing evaluation and the study drug administration occur on the same day, timing of the evaluation will be used to determine the pre- or post-dose. If timing is not available, the evaluation is considered pre- or post-dose based on the schedule of events for that assessment. For example, AEs and concomitant medication are considered post-baseline evaluations.

For the OLE baseline, it is defined as the last non-missing evaluation before the first dose of losmapimod in the OLE.

Relative study days will be calculated as:

(assessment date – first study drug administration date) + 1

if the assessment date is on the same day or after the first dosing date, otherwise:

(assessment date – first study drug administration date).

Where applicable, study day relative to first dose of losmapimod will also be provided and this will be calculated as:

(assessment date – first losmapimod administration date) + 1

if the assessment date is on the same day or after the first dosing date, otherwise:

(assessment date – first losmapimod administration date).

Both study days will be presented on all listings where appropriate.

Change from baseline will be computed as (post-baseline assessment value - baseline assessment value). Percent change from baseline will be computed as (change from baseline value/baseline assessment value)*100. For the OLE visits, change from baseline will be computed based on both baseline assessment value, baseline in the placebo-controlled treatment period and baseline in OLE.

4.5. Visit Windows

In general, data for assessments that are collected by scheduled visits will be mapped to visits that appear in the schedule of assessments per the protocol using the actual study day of assessment. Data mapped to scheduled visits will include all data collected up to the

reporting cut-off date and may include withdrawal visits, unscheduled visits, end of treatment, and safety follow-up visits.

Visit windows will be continuous from the midpoint between two consecutive study visits and will be dependent on the schedule of assessments for each variable independently. For analysis that includes presentation of data in the placebo-controlled treatment period, there is an exception in the Week 16 analysis window. This has been extended to allow for potentially delayed visit due to COVID-19 pandemic. An example of the Vital Signs visit window is given in Table 4-1. Visit windows for each variable will be constructed in the same manner.

Table 4-1: Visit Windows

Study Visit	Scheduled Day	Analysis Window
Baseline	1	<=1
Week 4	28	>1 to <=56
Week 12	84	>56 to <=98
Week 16	112	>98 to <=154
Week 24	168	>154 to <=210
Week 36	252	>210 to <=294
Week 48	336	>294 to <=378
Week 60	420	>378 to <=462
Week 72	504	>462 to <=546
Week 84	588	>546 to <=630
Week 96	672	>630 to <=714
Week 108	756	>714 to <=798
Week 120	840	>798 to <=882
Week 132	924	>882 to <=966
Week 144	1008	>966 to <=1050
Week 156	1092	>1050 to <=1134
Week 168	1176	>1134 to <=1218
Week 180	1260	>1218 to <=1302
Week 192	1344	>1302 to <=1386
Week 204	1428	>1386 to <=1470
Week 216	1512	>1470

4.6. Multiple Values

For summaries displayed by visit, multiple values for a given assessment within a time window will be handled as follows:

- Efficacy: The nearest non-missing value to the nominal timepoint will be assigned to the visit. If two values are equidistant from the nominal timepoint then the latest value will be selected.
- Safety: The earliest non-missing value within a visit window will be assigned to the visit.

For the PK and biomarker data, if the assay is believed to have failed for an assessment due to technical reasons, the sample will be re-run and the last/latest assessment date/time that is available will be used for the data analysis.

4.7. Subgroup

A subgroup analysis will be performed for the following subsets at baseline:

1) Sex (Male, Female)
2) Age (<50 years old and >=50 years old)

Endpoints for which the subgroup analysis will be performed are indicated in subsequent sections.

4.8. Sample Size

The sample size for OLE is determined by the number of subjects anticipated to roll over from the placebo-controlled treatment period. A total of 80 subjects have been enrolled in the placebo-controlled treatment period which is 4 subjects higher than the planned sample size of 76 subjects.

4.9. Randomization and Blinding

This non-randomized OLE includes subjects who previously completed the placebo-controlled treatment period part. No blinding will be performed (subjects will receive open-label losmapimod); however, subjects will remain blinded to their original treatment assignment from the placebo-controlled treatment period for the duration of the study. The Sponsor and/or its designee may be unblinded after all subjects have completed the Week 48 visit (or have discontinued) and the database from the placebo-controlled treatment period has been locked for statistical analyses. The [redacted] Biostatistics and Programming will be unblinded after the data for the placebo-controlled treatment period has been locked.

4.10. Analysis Set

4.10.1. Open-label Analysis Set

The open-label analysis set will consist of all subjects who complete 24 or 48 weeks of treatment in the placebo-controlled treatment period and receive at least 1 dose of open-label losmapimod in the OLE.

5. Subject Disposition

5.1. Disposition

A table will show the disposition of subjects with the number and percentage of subjects for the following categories:

- Subjects who entered OLE
- Subjects who completed the treatment in OLE
- Subjects who discontinued the treatment in OLE
- Subjects who completed the study
- Subjects who discontinued from the study

The reasons for study discontinuation will also be summarized.

Subject disposition data will also be presented in a listing.

5.2. Protocol Deviations

Protocol deviations will be summarized by deviation type. A listing of all protocol deviations will be provided as well. A separate presentation will be provided for significant deviations during the OLE period only.

6. Demographics and Baseline Characteristics

6.1. Demographics

A summary of demographics and baseline characteristics will be presented for subjects who entered the OLE. The demographic characteristics will consist of age (years), sex, race, and ethnicity. The baseline characteristics will consist of baseline height (cm), baseline weight (kg), baseline body mass index (BMI) (kg/m^2), and hand dominance (left or right). Body mass index is calculated as (body weight in kilograms) / (height in meters)^2. Age, baseline height, baseline weight, and baseline BMI will be summarized using descriptive statistics. The number and percentage of subjects by sex (Male, Female), race (White, African American, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific

Islander, and Other), ethnicity (Hispanic or Latino, Not Hispanic or Latino) and hand dominance will also be reported.

Subject demographic and baseline characteristics will also be presented in a listing.

6.2. Baseline Disease Characteristics

Baseline disease characteristics include the following parameters:

- FSHD repeat number (1, 2, 3, 4, 5, 6, 7, 8, and 9)
- FSHD repeat category (1 to 3 repeats, 4 to 9 repeats)
- Clinical severity score (RICCI score 2, 2.5, 3, 3.5, 4)
- FSHD history
    - Age of symptom (years)
    - First symptom
        - Weakness
        - Difficulty smiling
        - Reaching over head
        - Walking
        - Running
        - Keeping up with peers
        - Pain
        - Others
    - Age at diagnosis (years)
    - Pain related to FSHD

Baseline disease characteristics will also be presented in a listing.

7. Treatments and Medications

7.1. Concomitant Medications

All medications used within 28 days prior to the date of screening through safety follow-up will be collected on the CRF (case report form). All medications will be coded according to the World Health Organization Drug Dictionary (WHODD Global B3 Mar 2019 or higher). A concomitant medication is defined as any medication that is taken on or after the date of study drug administration regardless when the medication is started up to 7 days after the last dose date.

For the purpose of inclusion in concomitant medication tables, incomplete medication start and stop dates will be imputed as follows:

Missing start dates (where UK, UKN, and UNKN indicate unknown or missing day, month, and year, respectively):

- UK-MMM-YYYY: If the month and year are different from the month and year of administration of study drug, assume 01-MMM-YYYY. If the month and year are the same as the administration of study drug month and year and the end date (after any imputation) is on or after the administration of study drug, then assume the first day of the month of the administration of study drug. If the month and year are the same as month and year of the study drug administration and the end date (after any imputation) is prior to the study drug administration, then assume the first day of the month of the administration of the study drug for the start date;
- DD-UKN-YYYY/UK-UKN-YYYY: If the year is different from the year of the study drug administration, assume DD-JAN-YYYY/01-JAN-YYYY of the collected year. If the year is the same as study drug administration year and the end date (after any imputation) is on or after the study drug administration, then assume the date of the study drug administration. If the year is the same as the study drug administration and the end date (after any imputation) is prior to the first dose of study drug, then assume the first day of the month of the administration of the study drug for the start date.

Missing stop dates (where UK, UKN, and UNKN indicated unknown or missing day, month, and year, respectively):

- UK-MMM-YYYY: Assume the last day of the month;
- DD-UKN-YYYY: Assume DD-DEC-YYYY;
- UK-UKN-YYYY: Assume 31-DEC-YYYY.

If the start date is completely missing and end date is not prior to the study drug administration, then the medication will be classified as concomitant. If the start date is completely missing and the end date is within 30 days prior to the first dose of study drug, then the medication will be classified as prior. If the end date is missing, then the medication will be classified as ongoing. Medications for which the start and end dates are missing will be classified as concomitant.

Concomitant medications will be summarized by Anatomical Therapeutic Chemical (ATC) classification level 4 and preferred term (PT), respectively. When ATC classification level 4 is missing, the next available ATC level will be used as ATC level 4.

The total number of concomitant medications and the number and percentage of subjects with at least one concomitant medication throughout the duration of the study will be presented. A separate presentation will be done for concomitant medications taken during the placebo-controlled treatment period and OLE. The number and percentage of subjects taking each concomitant medication will be summarized by sequence of actual treatment received in combination with entry point of OLE and overall.

Data on concomitant medications will also be presented in a listing.

7.2. Study Treatments

7.2.1. Extent of Exposure

The duration of exposure to losmapimod is the total number of days a subject is exposed to losmapimod; this duration is the interval from the first dose date of losmapimod to last dose date of losmapimod (ie, calculated as the date of last dose of losmapimod minus the date of first dose of losmapimod + 1). If the last dose date of losmapimod is missing, or if a subject is lost to follow-up, but the drug accountability log confirms that the subject has taken losmapimod, the visit date following the last completed drug accountability log will be used.

The exposure to losmapimod will also be characterized by cumulative dose, which is defined as the cumulative number of losmapimod tablets taken in the placebo-controlled treatment period and OLE.

The duration of exposure to losmapimod will be summarized for all subjects who entered OLE using summary statistics according to the sequence of actual treatment received in combination with entry point of OLE. For the Placebo BID/Losmapimod 15 mg BID column, only the duration of exposure while on losmapimod will be summarized. The duration of exposure will then be classified into the following categories: < 8 weeks, >= 8 weeks, >= 16 weeks, >= 24 weeks, >=36 weeks, >=48 weeks, >=60 weeks, >=72 weeks, >=84 weeks, >=96 weeks, >=108 weeks, >=120 weeks, >=132 weeks, >=144 weeks, >=156 weeks, >=168 weeks, >=180 weeks, >=192 weeks, >=204 weeks, and >=216 weeks and will be presented as the number and percentage of subjects in each duration category.

The total cumulative dose for losmapimod in mg will be defined as the total number of losmapimod tablets taken across all study days times 7.5 mg if 2 tablets were given while times 15 mg if 1 tablet was given. Average daily dose of losmapimod will be defined as cumulative dose of losmapimod divided by total days on losmapimod. The average daily dose and cumulative dose will be summarized using summary statistics according to the sequence of actual treatment received in combination with entry point of OLE. For the Placebo BID/Losmapimod 15 mg BID columns, only the cumulative dose and average daily dose for losmapimod will be summarized.

A summary of each subject's exposure to losmapimod will also be presented in a listing.

7.2.2. Treatment Compliance

Losmapimod compliance will be calculated for each subject by taking into account whether a subject took all doses of losmapimod as instructed. The number of tablets taken will be calculated by subtracting the number of tablets returned from the number of tablets dispensed. The dosage taken will be calculated by summing the number of tablets taken times the corresponding tablet dosage.

The losmapimod compliance (%) for each visit will be calculated by dividing the total number of tablets taken up to the next visit by the total number of tablets prescribed at each visit and then multiplying by 100. Compliance (%) = [sum of ((total number of tablets dispensed – total number of tablets returned) * corresponding tablet dosage [mg]) / (number of days in visit interval * dosage [mg] prescribed per day)] * 100. The overall losmapimod compliance (%) will be calculated by dividing the total dosages [mg] taken at all visits by the total dosages [mg]prescribed for all visits and then multiplying by 100.

The overall losmapimod compliance will be summarized by sequence of actual treatment received in combination with entry point of OLE. For the Placebo BID/Losmapimod 15 mg BID columns, only the treatment compliance for losmapimod will be summarized.

The number and percentage of subjects in different percentage compliance categories (<80%, >=80% to <120%, and >= 120% compliant) will be presented.

8. Efficacy Analysis

Efficacy endpoints will be summarized over time showing both the placebo-controlled treatment period and OLE data.

8.1. MSK MRI Muscle Fat Fraction, Lean Muscle Volume and Muscle Fat Infiltration

Measurement of the extent of skeletal muscle tissue replacement by fat in FSHD patients will be done through automatic skeletal muscle segmentation for the 3D muscle volumes and fat fraction analysis via robust algorithms using Dixon imaging. Schedule of MRI assessments are described in Appendix 14.2.

A. **Longitudinal composite measures:** Longitudinal whole-body composite variables, incorporating pre-selected muscles, will be derived for longitudinal analysis of muscle fat fraction, lean muscle volume and muscle fat infiltration (MFF_{tot}, LMV_{tot}, and MFI_{tot} respectively), as described in Appendix 14.1. The scores will be derived by scientists at the MRI Service Provider (AMRA Medical Inc.).

   The longitudinal composite observations of relative change in LMV is sensitive to low overall LMV. Therefore, a criterion is required for exclusion of such observations. To ensure that the relative change in LMV is reliable, LMV_{ref} (LMV at reference timepoint) needs to fulfill one of the below:

   - Be at least 25 cl and consist of measurements from at least 2 muscles combined.
   - Be at least 50 cl with measurements from at least one muscle.

   Further, if the subject's individual muscles fulfill neither criteria, the change from reference timepoint in longitudinal composite scores for LMV (L), LMV (%), MFF (%), and MFI (%) are set to missing. If the individual muscles could fulfill at least one of the two bullets above, the change from reference time point in longitudinal composite scores for LMV (L), LMV (%), MFF (%), and MFI (%) are not set to missing.

   For each treatment sequence/entry point of OLE, descriptive statistics of MFF_{tot} , LMV_{tot}, and MFI_{tot} per visit as well as changes from baseline will be presented.

   To assess the efficacy of losmapimod in the placebo group after rollover into the OLE and the durability of efficacy in the losmapimod group, the mean change from baseline (+- SE) by visit of MFF_{tot}, LMV_{tot}, and MFI_{tot} will be graphically presented over both the placebo-controlled treatment period and OLE.

Three types of % change/year in longitudinal composite scores will be estimated:

(1) % change/year for losmapimod using data from both the placebo-controlled treatment period and OLE

Data while the subject is on losmapimod will be considered in the analysis. For subjects who were randomized to losmapimod at baseline, data from both the placebo-controlled treatment period and OLE will be included in the analysis. For subjects who were randomized to placebo and transitioned to losmapimod at OLE, their data under losmapimod are considered in the analysis. A linear mixed-effects model will be used to analyze the longitudinal composite scores for each treatment sequence, with intercept and time as random effects, and with adjustment for repeat number category and region (EU, USA, and Canada). An unstructured covariance matrix will be used to model the correlations between repeated measurements within each subject. In addition, the % change/year will be presented and will be derived as [(slope/baseline)*(365/T)*100] where baseline is the LS mean of the intercept and T is the duration of treatment with losmapimod minus 1.

(2) % change/year for the losmapimod group and placebo group using data from the placebo-controlled treatment period for subjects who completed 48 weeks of treatment in the placebo-controlled treatment period

A linear mixed-effects model will be used to analyze the longitudinal composite scores, with treatment sequence as a fixed effect, and intercept, time and treatment sequence-by-time interaction as random effects, adjusting for repeat number category and region (EU, USA, and Canada). An unstructured covariance matrix will be used to model the correlations between repeated measurements within each subject. Within-treatment sequence LS mean of slope and the associated SE, intercept and the associated SE, difference in the LS mean of slope and the associated 2-sided 95% CI and 2-sided p-value will be derived from the linear mixed-effects model and will be provided in the summary table. In addition, the % change/year will be presented. It will be derived as [(slope/baseline)*(365/T)*100] where baseline is the LS mean of the intercept and T is the duration of treatment with study drug minus 1. Difference in % change/year between treatment sequences will also be presented.

(3) % change/year for each treatment sequence using data from the OLE for subjects who completed 48 weeks of treatment in the placebo-controlled treatment period

The same approach as in (2) will be used to analyze the longitudinal composite scores in the OLE.

In estimating the three types of % change/year, if any model using an unstructured covariance matrix does not converge, an AR(1) covariance structure will be used

instead. If either unstructured or AR(1) covariance matrix does not lead to a convergent model, a compound symmetric covariance structure will be used instead.

The purpose of estimating % change/year for each treatment sequence in (2) and (3) above is to explore the possibility that earlier treatment with losmapimod is better than delayed treatment and that the placebo group's progression slows after treatment with losmapimod.

The change from baseline in the composite parameters will also be summarized by subgroups identified in Section 4.7 to evaluate consistency of treatment effects across the subgroups.

B. **Individual Muscles**: For each muscle location, a similar method will be used to analyze muscle fat fraction (%), lean muscle volume (L), and muscle fat infiltration (%) per visit as well as changes from baseline.

C. **Cross-sectional composite measures**: The cross-sectional composite scores will be used to correlate the results with Clinical Outcome Assessments (i.e., TUG, FSHD TUG and RWS). The convention that will be used to get extremity equivalent of the cross-sectional results is provided in Table 8-1.

Table 8-1. Extremity Equivalent of MRI Cross-sectional Results.

MRI Cross-sectional Results	Equivalent Extremity
TUG Cross-sectional	Lower extremity (LE)
FSHD TUG	All Muscles
RWS Dominant Cross-sectional	Dominant upper extremity
RWS Non-Dominant Cross-sectional	Non-Dominant upper extremity

The muscles considered for each of the cross-sectional composite scores are presented in Table 8-2.

Table 8-2. Muscles Considered in the MRI Cross-sectional Scores

Test	Muscles		
	Upper Extremity	Trunk	Lower Extremity
FHSD TUG	Supraspinatus Infraspinatus	Pectoralis Major Rhomboideus	Quadriceps Hamstrings

Test	Muscles		
	Upper Extremity	**Trunk**	**Lower Extremity**
	Subscapularis Teres Minor Deltoid Biceps Brachii Triceps Brachii	Latissimus Dorsi & Teres Major Trapezius Serratus Anterior Paraspinal (C3-Sacrum)	Adductors Tibialis Anterior Gastrocnemius Medialis
Classic TUG	N/A	N/A	Quadriceps Hamstrings Adductors Tibialis Anterior Gastrocnemius Medialis
RWS	Supraspinatus Infraspinatus Subscapularis Teres Minor Deltoid Biceps Brachii Triceps Brachii	Pectoralis Major Rhomboideus Latissimus Dorsi & Teres Major Serratus Anterior	N/A

Spearman correlation coefficients will be used to assess relationships between the cross-sectional composite scores and classical and FSHD TUG and RWS results by visit. The Spearman correlation coefficient and p-value will be calculated and presented in a table. This will also be graphically presented using scatterplots. Specifically, the following relationships will be assessed:

- All muscles vs. FSHD-TUG
- LE vs. Classical TUG
- Dominant upper extremity vs. Dominant RWS
- Non-Dominant upper extremity vs. Non-Dominant RWS

8.2. Clinical Outcome Assessments

8.2.1. Reachable Workspace With and Without Weights

The reachable workspace (RWS) is a 3-dimensional sensor-based system (using a single depth-ranging sensor) that can unobtrusively detect an individual's ability to reach in various directions above and below the shoulder, and reflects an individual global upper extremity

function. The evaluation will be performed with and without weights and on both the right and left arms. Schedule of RWS assessments are described in Appendix 14.2.

The absolute total RWS surface envelope area (m^2) as well as areas for each of the quadrants will be calculated and provided by a vendor with no access to treatment assignment information from the placebo-controlled treatment period of the study. The reachable workspace relative surface area (RSA) represents the portion of the unit hemisphere that is covered by an individual's arm movement.

For each treatment sequence/entry point of OLE, descriptive statistics of RSA results per visit as well as the change from baseline will be presented by quadrant, upper quadrants (Q1+Q3), total area with Q5 (Q1+Q2+Q3+Q4+Q5), and total area without Q5 (Q1+Q2+Q3+Q4) for the assessment with weights and without weights, and by dominant arm, non-dominant arm and average from two arms. Similar methods will be used to analyze the change from baseline in RSA for all RSA measures. For upper quadrants, total area with Q5 and without Q5, the average results from two arms will be calculated as:

- first calculate the sum on each arm,
- then calculate the average from two arms.

If results are missing on one arm and non-missing on the other arm, the average result will be equal to the non-missing result from one arm.
To assess the efficacy of losmapimod in the placebo group after rollover into the OLE and the durability of efficacy in the losmapimod group, the mean change from baseline (+- SE) by visit of all RSA measures will be graphically presented over both the placebo-controlled treatment period and OLE.

Three types of % change/year in RSA will be estimated. The analysis approaches will be similar to those of the MRI longitudinal composite scores in Section 8.1. Separate models will be run for each quadrant (Q1, Q2, Q3, Q4 and Q5), upper quadrants (Q1+Q3), total area with Q5 (Q1+Q2+Q3+Q4+Q5), and total area without Q5 (Q1+Q2+Q3+Q4) with and without weights, and for the dominant arm, non-dominant arm and average from two arms.

Invalid RWS data points due to software issues will be flagged and excluded from all analyses.

8.2.2. Classic and FSHD TUG

The TUG test, which is used to assess a person's mobility, requires dynamic balance. The TUG measures the time that a person takes to rise from a chair, walk 3 meters, turn around, walk back to the chair, and sit down. The FSHD TUG adds to the classic TUG by incorporating trunk and upper extremity components (supine to sit and sit to supine). The FSHD TUG will capture total completion time and completion times for each segment (supine to sit, sit-to-stand then walk-and return to-sit, and sit to supine). Each test is done

twice per visit. Schedule of classic and FSHD TUG assessments are described in Appendix 14.2. The average of Trial 1 and Trial 2 assessments at each visit will be derived for both the classic TUG completion time and each of the FSHD TUG completion times (ie, supine to sit, sit-to-stand then walk- and return to-sit, sit to supine, and total) and will be used for the analysis.

For each treatment sequence/entry point of OLE, descriptive statistics of classic TUG average completion time and FSHD TUG average completion times in seconds per visit as well as the change from baseline will be provided in tables. Descriptive statistics of FSHD TUG average completion times will be presented for each segment (supine to sit, sit-to-stand then walk-sit, sit to supine, and total). Similar methods will be used to analyze the change from baseline in FSHD TUG average completion times.

Similar analysis will also be conducted for each of the individual components of the FSHD TUG.

To assess the efficacy of losmapimod in the placebo group after rollover into the OLE and the durability of efficacy in the losmapimod group, the mean change from baseline (+- SE) by visit of classic TUG will be graphically presented over both the placebo-controlled treatment period and OLE.

Three types of % change/year in classic TUG will be estimated. The analysis approaches will be similar to those of the MRI longitudinal composite scores in Section 8.1.

8.2.3. Manual Dynamometry

Qualitative isometric dynamometry (hand-held dynamometer) will be used to assess the skeletal muscle strength of study subjects in both the upper and lower limbs bilaterally. Shoulders, flexors and extensors in the elbow, knees, and ankles as well as the grip bilaterally will be measured at each applicable visit. Isometric dynamometry measures the static muscle strength without any movement. The schedules of manual dynamometry assessments are described in Appendix 14.2.

Total dynamometry results on all muscles combined, upper extremity, lower extremity are derived; average and maximum weight in kilogram per visit are also derived for analysis. For each treatment sequence/entry point of OLE, descriptive statistics of total, average and maximum weight in kilogram per visit as well as the change from baseline and percent change from baseline will be presented overall and according to assessment (dominant shoulder abductors, non-dominant shoulder abductors, dominant elbow flexors, non-dominant elbow flexors, dominant elbow extensors, non-dominant elbow extensors, right

ankle dorsiflexors, left ankle dorsiflexors, dominant hand grip, and non-dominant hand grip). The averages from dominant and non-dominant averages and maximums on all assessments will be analyzed similarly.

Similar analysis will be done for total average manual dynamometry for: (a.) all muscles combined; (b.) upper extremity strength, in the shoulders and elbows combined; and (c.) lower extremity strength, which includes right ankle dorsiflexors, and left ankle dorsiflexors muscles combined.

To assess the efficacy of losmapimod in the placebo group after rollover into the OLE and the durability of efficacy in the losmapimod group, the mean change from baseline (+- SE) by visit of all manual dynamometry measures will be graphically presented over both the placebo-controlled treatment period and OLE.

Three types of % change/year in dynamometry results, overall and per assessment, will be estimated. The analysis approaches will be similar to those of the MRI longitudinal composite scores in Section 8.1.

8.2.4. MFM Domain 1

The MFM scale, which assesses the severity of the motor deficit, provides a clinician's assessment of functionality impairment for standing and transfers. Domain 1 has 13 items in version 1 and 15 items in version 3 of the protocol with each item scored from 0 to 3. The MFM Domain 1 score corresponds to the sum of the item scores divided by the maximum score for this dimension and multiplied by 100 (ie, sum of scores/39*100 for 13 items questionnaire and sum of scores/45*100 for the 15 items questionnaire). Schedule of MFM assessments are described in Appendix 14.2.

For each treatment sequence/entry point of OLE, descriptive statistics of the MFM Domain 1 scores (individual item scores and Domain 1 score) per visit as well as the change from baseline will be presented.

Shift in MFM Domain 1 scores from baseline will also be presented. Baseline results will be categorized into 0 to 25, >25 to 50, >50 to 75, >75 to 100. Post baseline results will be presented as shift to high, no change, or shift to low depending on the change relative to baseline. For example, if the subject has baseline MFM Domain 1 score belonging to category >25 to 50 and the post baseline MFM Domain 1 score is 54, then, the post baseline result considered as shift to high.

8.2.5. FSHD-HI

The FSHD-HI is an FSHD-specific patient-reported measure of disease burden on activities of daily living, quality of life, and symptom prevalence and severity. The measure consists of a questionnaire with 116 items developed from qualitative interviews of patients. The 14 subscales in the FSHD-HI measure patients' perception of their ambulation and mobility, hand function, shoulder and arm function, emotional health, back/chest/abdomen strength, fatigue, pain, eating function, ability to do activities, communication ability, satisfaction in social situations, performance situations, body image and cognition. The 116 items are combined into a total score; the score is then transformed onto a percentage scale, with 100 representing maximal disability, and lower scores representing decreasing disability. This FSHD-HI total score will be calculated by a separate vendor. This score, along with the 14 subscale scores, will be assessed as shown in the schedule described in Appendix 14.2.

For each treatment sequence/entry point of OLE, descriptive statistics of the FSHD-HI total and subscale scores per visit as well as the change from baseline will be presented. Similar methods will be used to analyze the change from baseline in FSHD-HI subscale scores.

8.2.6. PGIC

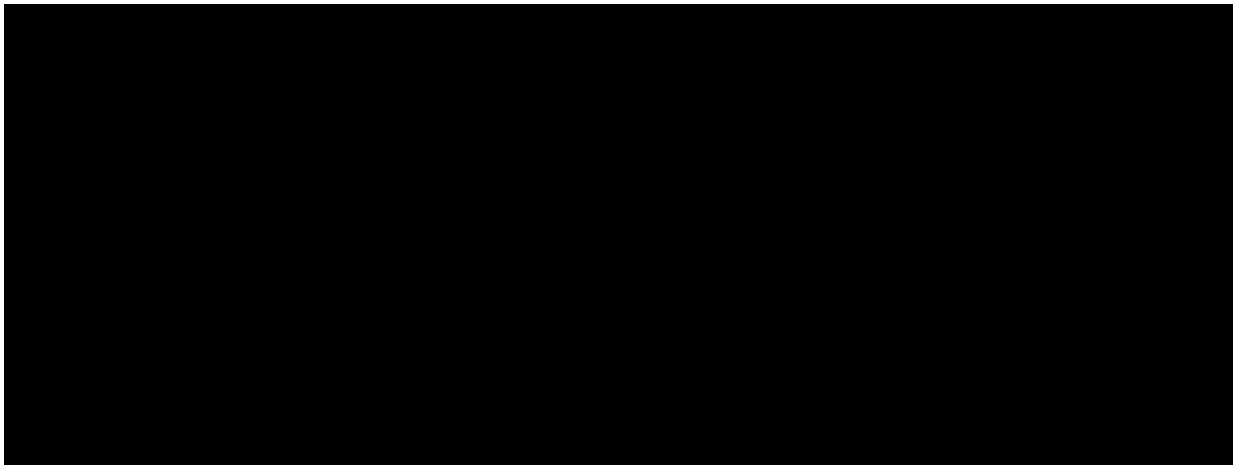
The PGIC will be assessed to obtain the subject's rating of overall improvement. The rating has the following scores: 1= Very much improved, 2= Much improved, 3= Minimally improved, 4= No change, 5= Minimally worse, 6= Much worse, 7=Very much worse. The schedule of PGIC assessments is described in Appendix 14.2.

Responses of 1, 2, and 3 will be considered "improved", while responses of 4, 5, 6, and 7 will be considered not improved. Alternatively, responses of 1, 2, 3 and 4 will be considered as not worsened, and responses of 5, 6 and 7 will be considered as worsened. For each treatment sequence/entry point of OLE, descriptive statistics of PGIC values and PGIC response categories will be presented.

To assess the efficacy of losmapimod in the placebo group after rollover into the OLE and the durability of efficacy in the losmapimod group, the mean (+- SE) by visit of PGIC will be graphically presented over both the placebo-controlled treatment period and OLE.

8.3. Inflammatory, Immune, Apoptotic, and Muscle Disease Transcripts

The analysis of these exploratory endpoints will be described in a separate document.



9. Safety Analysis

9.1. Adverse Events

A treatment-emergent AE (TEAE) is defined as an AE that meets any of the following conditions:

- begins on or after the first dose of study drug and before 8 days after the stop of study drug;
- begins before the first dose of study drug and worsens on or after the first dose of study drug and before 8 days after the stop of study drug;
- is completely missing an onset date and end date;
- is completely missing an onset date and the end date is on or after the first dose of study drug.

For the purpose of inclusion in TEAE tables, incomplete AE onset and end dates will be imputed as follows:

Missing onset dates (where UK and UKN indicate unknown or missing day and month respectively):

- UK-MMM-YYYY: If the AE month and year are different from the month and year of the first dose of study drug, assume 01-MMM-YYYY. If the month and year are the same as the first dose of study drug month and year and the AE end date (after any imputation) is on or after the first dose of study drug, then assume the date of the first dose of study drug. If the AE month and year are the same as the first dose of study drug month and year and the AE end date (after any imputation) is prior to the first dose of study drug, then assume the end date for the onset date.
- DD-UKN-YYYY/UK-UKN-YYYY: If the AE year is different from the year of first dose of study drug, assume DD-JAN-YYYY/01-JAN-YYYY of the collected year. If the AE year is the same as the first dose of study drug year and the AE end date

(after any imputation) is on or after the first dose of study drug, then assume the date of the first dose of study drug. If the year is the same as the first dose of study drug and the AE end date (after any imputation) is prior to the first dose of study drug, then assume the end date for the onset date.

Missing end dates (where UK and UKN indicate unknown or missing day and month respectively):

- UK-MMM-YYYY: Assume the last day of the month;
- DD-UKN-YYYY: Assume DD-DEC-YYYY;
- UK-UKN-YYYY: Assume 31-DEC-YYYY.

All AEs will be classified by SOC and PT according to the MedDRA version 22.0 or higher.

An overview summary of the number and percentage of subjects with any TEAE, serious TEAE, study drug-related TEAE, study drug-related serious TEAE, TEAE leading to treatment discontinuation, TEAE leading to study withdrawal, and AE leading to death throughout the duration of the study will be provided. An TEAE is considered as study drug-related if the relationship assessment provided by the investigator is "Possibly Related", "Probably Related", "Definitely Related", or missing.

In addition, the number and percentage of subjects with at least one AESI will be presented. Adverse events of special interest for this study include liver tests that meet the criteria for potential drug-induced liver injury (DILI) in accordance with the US Food and Drug Administration (FDA) "Guidance for Industry-Drug-Induced Liver Injury: Premarketing Clinical Evaluation". Further details of liver tests and criteria are described in Section 9.2.2.

A separate presentation, unless otherwise specified, will be provided for TEAEs that occurred during the placebo-controlled treatment period and OLE. A total column will be presented for tables showing TEAEs during the OLE.

9.1.1. Incidence of TEAEs

Summaries of the total number of TEAEs and the number and percentage of subjects with at least one TEAE will be provided. The number and percentage of subjects and the number of events will also be presented by SOC and PT. At each level of subject summarization, a subject is counted once within each PT if the subject reported one or more events.

The summary of TEAEs will also be presented in descending order from the SOC with the highest total incidence (that is, summed across all treatment groups) to the SOC with the lowest total incidence. If the total incidence for any two or more SOCs is equal, the SOCs will be presented in alphabetical order. Within each SOC, the PTs will be presented in alphabetical order.

An additional summary will be presented by PT only. This summary will be presented in descending order from the PT with the highest total incidence to the PT with the lowest total incidence.

All AEs will also be presented in a listing.

9.1.2. Relationship of TEAEs to Study Drug

A summary of TEAEs by maximum relationship to study drug will be presented in a table by incidence of occurrence. The investigator will provide an assessment of the relationship of the event to the study drug. The possible relationships are "Unlikely Related", "Possibly Related", "Probably Related", and "Definitely Related". In the TEAE by maximum relationship table, if a subject reports multiple occurrence of the same TEAE, only the most related occurrence will be summarized. All AEs that have a missing relationship will be presented in the summary table as "Missing", but will be presented in the data listing with a missing relationship.

The AE data will be categorized and presented by SOC, PT, and relationship in the same manner as described in Section 9.1.1.

9.1.3. Severity of TEAE

A summary of TEAEs by maximum severity will be presented in a table. The severity that will be presented represents the most extreme severity captured on the CRF page. The possible severities are "Mild", "Moderate", and "Severe". In the TEAE by maximum severity table, if a subject reported multiple occurrences of the same TEAE, only the most severe occurrence will be summarized. AEs that are missing severity will be presented in tables as "Missing", but will be presented in the data listing with a missing severity.
The AE data will be categorized and presented by SOC, PT, and severity in the same manner as described in Section 9.1.1.

9.1.4. Serious TEAEs

The seriousness of an AE should be assessed independently by the Investigator. An SAE is defined as any untoward medical occurrence that at any dose results in death, is life-threatening, is a congenital anomaly/birth defect, requires in-patient hospitalization or prolongation, or results in significant disability.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered SAEs when, based upon medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

SAE data will be presented by SOC and PT in the same manner as described in Section 9.1.1.

9.1.5. TEAEs Leading to Treatment Discontinuation

A summary of TEAEs that caused treatment discontinuation will be presented in a table. At each level of subject summarization, a subject is counted once if the subject reported one or more events.

TEAE leading to treatment discontinuation data will be presented by SOC and PT in the same manner as described in Section 9.1.1.

9.1.6. TEAEs Leading to Study Withdrawal

A summary of TEAEs that led to study discontinuation will be presented in a table. At each level of subject summarization, a subject is counted once if the subject reported one or more events.

TEAE leading to study discontinuation data will be presented by SOC and PT in the same manner as described in Section 9.1.1.

9.1.7. Death

A summary of TEAEs where the answer to ‘Outcome’ in the AE form is ‘Death Related to Adverse Event’ will be presented in a table.

Death data will be presented by SOC and PT in the same manner as described in Section 9.1.1.

9.2. Clinical Laboratory Evaluations

Results from laboratory assessments will be summarized over time showing both the placebo-controlled treatment period and OLE data.

9.2.1. Hematology

The following laboratory tests will be included: hemoglobin (including mean corpuscular volume), mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hematocrit, red blood cell count, total white blood count, platelet count, differential blood counts, including basophils, eosinophils, neutrophils, lymphocytes, and monocytes.

Summary tables presenting observed values and changes from baseline will be presented for the following hematologic tests: hemoglobin, red blood cell count, hematocrit, total white blood cell count, lymphocyte count, neutrophil count, basophil count, eosinophil count, and platelet count. Changes from baseline to each scheduled post-baseline visit will be presented. All hematology data by subject will also be presented in a listing.

The clinical assessment of 'Low', 'Normal', or 'High' relative to the reference range will be summarized comparing the baseline results to the minimum and maximum values post-baseline in separate shift tables for those subjects with results at both baseline and post-baseline visits.

9.2.2. Serum Chemistry

The following laboratory tests will be included**:** glucose, sodium, potassium, calcium, inorganic phosphate, total protein, albumin, blood urea nitrogen, creatinine, total bilirubin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase, and creatinine phosphokinase.

Summary tables presenting observed values and changes from baseline will be presented for the following serum chemistry tests: direct bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, and gamma-glutamyltransferase. Changes from baseline to each scheduled post-baseline visit will be presented. All chemistry data by subject will also be presented in a listing.

The clinical assessment of 'Low', 'Normal', or 'High' relative to the reference range will be summarized comparing the baseline results to the minimum and maximum values post-baseline in separate shift tables for those subjects with results at both baseline and post-baseline visits.

Results indicating liver-related abnormalities (i.e., ALT, AST, Total Bilirubin, and/or ALP) will be summarized separately. A newly notable laboratory abnormality is defined as an abnormality observed post baseline that meets the notable criteria in Table 9-1 and that did not exist at baseline. Subjects can still meet the criteria for a newly notable laboratory abnormality if the baseline value is missing. The table below displays the general variables and thresholds of interest. Subjects are considered to have notable laboratory abnormalities if his/her response falls within the specified definitions at least once during the treatment period.

Table 9-1: Notable Criteria for Laboratory Data Abnormalities – Liver Function Tests

Laboratory Variable	SI Units
AST	≥3 x ULN
ALT	≥3 x ULN
Total Bilirubin	≥2 x ULN

A summary of liver tests that meet the criteria for potential drug induced liver injury (DILI) will be presented. A potential DILI or Hy's law case is defined as ALT or AST >= 3 x ULN and total bilirubin >= 2 x ULN and ALP <= 2 x ULN.

9.2.3. Urinalysis

The following urine laboratory tests will be included*:* leukocytes, blood, nitrite, protein, urobilinogen, bilirubin, pH, specific gravity, ketones, and glucose*.*

Summary tables presenting observed values and changes from baseline will be presented for the following urinalysis tests: glucose, blood and protein. Changes from baseline to each scheduled post-baseline visit will be presented.

All urinalysis data by subject will be presented in a listing.

9.3. Vital Sign Measurements

Summary tables will be presented for vital sign data, including pulse rate, respiration rate, blood pressure, temperature, height, weight and BMI. BMI will be calculated based on the collected height and weight if missing. Observed results at each visit as well as the change from baseline to each post-dose assessment will also be presented. Results from both the

placebo-controlled treatment period and OLE will be summarized over time. All vital sign data by subject will also be presented in a listing.

9.4. Physical Examination

A table will summarize physical examination results. Status of a body system and any finding associated with the body system as normal, abnormal, or not done will be captured at screening and safety follow-up. Results from both the placebo-controlled treatment period and OLE will be summarized over time. Physical examination results for all subjects will also be presented in a listing.

9.5. Electrocardiogram

Subjects will have a standard 12-lead ECG performed during the study. Results from both the placebo-controlled treatment period and OLE will be summarized over time. Electrocardiogram data for all subjects will be presented in a listing.

Each subject's maximum on-treatment QTcF interval will be categorized as $\leqslant 450$, > 450 to $\leqslant 480$, > 480 to $\leqslant 500$, and > 500 msec. The number and percentage of subjects in each category will be presented by treatment group. Each subject's maximum on-treatment change from baseline in QTcF interval will be categorized as < 0, $\geqslant 0$ to $\leqslant 30$, > 30 to $\leqslant 60$, >60 msec. The number and percentage of subjects in each category will be presented by treatment group.

ECG data for all subjects will also be presented in a listing.

10. Pharmacokinetics

By-subject listing of pharmacokinetic blood sample and muscle sample collection times as well as derived sampling time deviations will be provided. Losmapimod plasma and muscle concentrations will be summarized using descriptive statistics (n, mean, standard deviation, minimum, median, maximum, coefficient of variation) by scheduled time point. Concentrations that are below the limit of quantitation (BLQ) will have a value of LLOQ value divided by 2 in the computation of descriptive statistics. Mean concentration-time data will be graphically presented. Results from both the placebo-controlled treatment period and OLE will be summarized over time.

Predose samples that are missing will be assigned as missing.

Concentrations assigned a value of missing will be omitted from the calculation of descriptive statistics. If 50% or more of the values are BLQ at one scheduled time point, the arithmetic mean will be reported as BLQ.

The individual and mean plasma concentrations and the individual and mean concentrations in skeletal muscle biopsies will be presented by scheduled time point in figures on linear scales.

11. Modification from the Planned Statistical Analysis in Protocol

11.1. Interim Analysis

Interim analyses may occur at any time during the OLE as determined by Fulcrum. In general, the unblinded [redacted] Biostatistics and Programming team will use unblinded data to program tables, listings and figures (TLFs) based on the SAP.

11.2. Open-label Analysis Set

The protocol defines the Open-label analysis set for subjects who complete 24 weeks of treatment in the placebo-controlled treatment period and receive at least 1 dose of open-label losmapimod in the OLE.
This analysis set will also include subjects who complete 48 weeks of treatment in the placebo-controlled treatment period and receive at least 1 dose of open-label losmapimod in the OLE.

12. Safety Review Committee (SRC)

The SRC will continue to meet and review the data from the OLE. These meetings will be planned at regular intervals. Details about data to be presented will be provided in the SRC Charter. The SRC may convene ad hoc meetings based on rates of SAEs if safety concerns arise during the trial. After its assessment, the SRC will recommend continuation, modification or termination of the clinical trial.

The [redacted] Biostatistics and Programming will prepare the safety tables, listings and/or figures using the actual randomization and materials/kits schedule.

13. References

Han J, Kurillo G, Abresch R, et al. Reachable Workspace in Facioscapulohumeral muscular dystrophy (FSHD) by Kinect. Muscle Nerve. 2015 February ; 51(2): 168-175

Lemmers RJ, Wohlgemuth M, Frants RR, et al. Contractions of D4Z4 on 4qB subtelomeres do not cause facioscapulohumeral muscular dystrophy. Am J Hum Genet. 2004;75:1124-30.

Lemmers RJ, van der Vliet PJ, Klooster R, et al. A unifying genetic model for Facioscapulohumeral Muscular Dystrophy. Science. 2010;329(5999):1650-3.

Lemmers RJ, Tawil R, Petek LM, et al. Digenic inheritance of an SMCHD1 mutation and an FSHD-permissive D4Z4 allele causes facioscapulohumeral muscular dystrophy type 2. Nat Genet. 2012;44(12):1370-4.

Ruiz-Cortes X, Ortiz-Corredor F, Mendoza-Pulido C, Reliabilty of home-based, motor function measure in hereditary neuromuscular diseases. Journal of International Medical Research. 2017, Vol. 45 (I) 261-271

Statland JM and Tawil R. Risk of functional impairment in facioscapulohumeral muscular dystrophy. Muscle Nerve. 2014;49(4):520-7.

Statland JM, Shah B, Henderson D, et al. Muscle pathology grade for facioscapulohumeral muscular dystrophy biopsies. Muscle Nerve. 2015;52(4):521-6.

Statland JM, Odrzywolski KJ, Shah B, et al. Immunohistochemical characterization of facioscapulohumeral muscular dystrophy muscle biopsies. J Neuromuscul Dis. 2015; 2(3):291-9.

Tawil R, Forrester J, Griggs RC, et al. Evidence for anticipation and association of deletion size with severity in facioscapulohumeral muscular dystrophy. The FSH-DY Group. Ann Neurol. 1996;39 (6):744–48.

Tawil R, Kissel JT, Heatwole C, et al. Evidence-based guideline summary: Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the

American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine. 2015;85(4):357-64.

14. Appendices

14.1. Derivation of MRI Composite Scores

Input to the Statistical Plan for FSHD analysis

Muscle categorization

Each muscle is categorized into one of three categories[1]:

A. 'Normal' muscles are normal appearing (low MFI and MFF, muscle likely unaffected by disease)
B. 'Affected' muscles have a likely disease involvement (intermediate MFI and MFF)
C. 'End-stage' corresponds to that more than 50% of the muscle tissue has been replaced by fat, and most of the functional capacity is likely lost

Muscle category	MFF criteria		MFI criteria
A. Normal	MFF < 50%	AND	MFI < 10%
B. Affected	MFF < 50%	AND	MFI ≥ 10%
C. End-stage	MFF ≥ 50%	-	-

Quality control of measurements

Trained anatomical imaging experts evaluate the signal quality in each muscle. If a muscle is not analyzable, that muscle is marked as not analyzable and no measurements will be extracted from it. For cross-sectional analysis minor quality issues are accepted, but not for longitudinal analysis. Hence, as seen below, we'll use different statistical inclusion parameters depending on if we are doing a cross-sectional or longitudinal analysis.

Statistical inclusion parameters

The muscle categorization and quality control results are summarized in 3 statistical inclusion parameters which will be provided for each muscle:

- Statistical Inclusion Category: Can take the values **A**, **B** or **C**, which correspond to 'Normal', 'Affected' and 'End-stage'. Abbreviated SI_{cat} in equations.
- Statistical Inclusion Cross-sectional: Can take the values **0** or **1** (0 if there are major signal quality issues indicating unreliable measurement, 1 otherwise). Abbreviated SI_{cross} in equations.
- Statistical Inclusion Longitudinal: Can take the values **0** or **1** (0 if there are any signal quality issues, including minor, 1 otherwise). Abbreviated SI_{long} in equations.

Note: In general, if a SI parameter is 'Unable to Assess', 'NA' or '0', that muscle should be excluded from the corresponding data analysis. . As for other muscle measurements, the SI parameters will have a corresponding 'Quality Issues' column – these columns may be ignored.

Whole-body combined measurements

Cross-sectional analysis

MRI-based measurements from multiple muscles is combined to obtain global measurements of disease affection for correlation to disease severity or functional test scores in cross-sectional data:

$$LMV_{tot} = \sum_{i \in muscles} SI_{cross,i} \cdot LMV_i$$

$$MFI_{tot} = \frac{\sum_{i \in muscles} SI_{cross,i} \cdot MFI_i \cdot LMV_i}{\sum_{i \in muscles} SI_{cross,i} \cdot LMV_i}$$

$$MFF_{tot} = 1 - \frac{\sum_{i \in muscles} SI_{cross,i} \cdot LMV_i}{\sum_{i \in muscles} SI_{cross,i} \cdot TMV_i}$$

MFF_{tot} is likely to correlate best with functional tests as it reflects global muscle-to-fat replacement, while interpretation of total LMV at only one timepoint requires reference data for normal total LMV that is not available at the moment. Note that muscles are included regardless of category (A, B

[1] Note that AMRA® Researcher is for research purposes only, and the names of these categories do not correspond to any form of diagnosis.

14.2. Protocol Version 4.0 Schedule of Study Procedures: Open-Label Extension (Visits will Occur Quarterly Until Study Drug Approval or Study is Discontinued)

Procedure	Week 60 Week 108 Week 156 Week 204	Week 72 Week 120 Week 168 Week 216	Week 84 Week 132 Week 180	Week 96 Week 144 Week 192	ET Visit[a]	Safety Follow-Up 7 Days After the Last Dose of Study Drug
Visit Window (days)[b]	**±7**	**±7**	**±7**	**±7**		**±3**
Weight, height, and BMI[c]		X				
Urine pregnancy test[e]	X	X	X	X	X	X
Vital signs[f]	X	X	X	X	X	X
Physical examination[g]						X
Standard 12-lead ECG[h]	X	X	X	X	X	X
Serum chemistry	X	X	X	X	X	X
Hematology	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X
MSK MRI[i]		X		X	X[j]	
PK sampling[k]	X	X	X	X	X	
RWS	X	X	X	X	X	X
TUG (classic and FSHD)	X	X	X	X	X	X
Manual dynamometry	X	X	X	X	X	X
MFM Domain 1	X	X	X	X	X	
FSHD-HI questionnaire	X	X	X	X	X	X
PGIC questionnaire	X	X	X	X	X	X
Clinic visit	X	X	X	X	X	X
Study drug dispensation[m]	X	X	X	X		

Procedure	Week 60 Week 108 Week 156 Week 204	Week 72 Week 120 Week 168 Week 216	Week 84 Week 132 Week 180	Week 96 Week 144 Week 192	ET Visit[a]	Safety Follow-Up 7 Days After the Last Dose of Study Drug
Study drug count	X	X	X	X	X	
Concomitant medications[n]	*Continuous from signing the ICF through the safety follow-up visit*					
Concomitant treatments and procedures	*Continuous from signing the ICF through the safety follow-up visit*					
Adverse event monitoring	*Continuous from signing the ICF through the safety follow-up visit*					

Abbreviations: BMI, body mass index; ECG, electrocardiogram; ET, early termination; FSHD, facioscapulohumeral muscular dystrophy; FSHD-HI, Facioscapulohumeral Muscular Dystrophy Health Index; ICF, informed consent form; MFM, Motor Function Measure; MRI, magnetic resonance imaging; MSK, musculoskeletal; OLE, open-label extension; PGIC, Patients' Global Impression of Change; PK, pharmacokinetic(s); RWS, Reachable Workspace; TUG, Timed Up and Go.

[a] If a subject prematurely discontinues study treatment during the OLE, they will be encouraged to remain in the study and continue with all other aspects of the study. If a subject decides to prematurely discontinue study treatment during the OLE and not continue with all other aspects of the study, they will be considered to have withdrawn from the study. If a subject withdraws from the study during the OLE, they will be asked to complete the ET visit as soon as possible after the decision to terminate study participation and to complete the safety follow-up visit 7 (±3) days after their last dose of study drug. If the ET visit will be scheduled more than 7 days after the last dose of study drug, the safety follow-up and ET visits may be combined, with no duplication of assessments required.

[b] Scheduled visits may be split over 2 days if required, with a maximum of 5 business days in between visits. Unscheduled visits may be performed if clinically indicated. Subjects can travel for MRI or muscle biopsy if needed, but the use of a study-approved MRI scanner should be consistent during the trial.

[c] Weight and height will be measured and BMI will be calculated once a year (ie, Week 48, Week 96, Week 144, etc.). Weight and height will be measured with shoes off and preferably with the same balance.

[d] [redacted]

[e] Urine pregnancy tests will be performed for all female subjects of child-bearing potential before dispensation of study drug. If pregnancy is found, subjects must be terminated from the study effective immediately.

[f] Vital signs (pulse rate, respiration rate, blood pressure, and temperature) will be collected after the subject has been seated or recumbent for at least 5 minutes and before any 12-lead ECG assessment or blood sampling is performed.

[g] Physical examination at the safety follow-up visit includes an evaluation of body systems, including but not limited to the following: skin; head, eyes, ears, nose, and throat; respiratory system; cardiovascular system; abdomen (liver, spleen); lymph nodes; neurological system; and MSK system. Symptom-directed physical examinations can occur at any time during the study if triggered by adverse events or if deemed necessary by the investigator.

[h] Twelve-lead ECGs will be performed after subjects have been recumbent for at least 5 minutes. Twelve-lead ECGs will be performed after the measurement of vital signs and before any procedures that may affect heart rate (eg, blood sampling).

[i] Subjects will be screened for any contraindications to MRI as per clinic standard practice.

[j] The MRI at the ET visit will not be repeated if an MRI was completed during the previous 12 weeks.

[k] Blood samples for PK will be collected after dosing at each clinic visit, preferably ≥1 hour after dosing.

[l] [redacted]

[m] The appropriate amount of study drug supply (losmapimod) will be given to the subject at each applicable visit to allow for dosing until their next scheduled study visit plus additional tablets to cover the visit window or additional study drug will be provided to the subject via a courier, as applicable. Study drug (losmapimod) will be administered as 2 tablets taken twice daily and should be taken with food.

[n] All medications taken within 28 days before screening through the safety follow-up visit will be recorded.

14.3. Protocol Version 5.0 Schedule of Study Procedures: Schedule of Events: Open-Label Extension (Visits Will Occur Quarterly Until 90 Days After Commercial Drug Availability Post Regulatory Approval or Study is Discontinued)

Procedure	**Week 60 Week 108 Week 156 Week 204 etc.**	**Week 72 Week 120 Week 168 Week 216 etc.**	**Week 84 Week 132 Week 180 etc.**	**Week 96 Week 144 Week 192 etc.**	**ET Visit[a]**	**Safety Follow-Up 7 Days After the Last Dose of Study Drug**
Visit Window (days)[b]	**±7**	**±7**	**±7**	**±7**		**±3**
Weight, height, and BMI[c]		X				
Urine pregnancy test[e]	X	X	X	X	X	X
Vital signs[f]	X	X	X	X	X	X
Physical examination[g]						X
Standard 12-lead ECG[h]	X	X	X	X	X	X
Serum chemistry	X	X	X	X	X	X
Hematology	X	X	X	X	X	X
Urinalysis	X	X	X	X	X	X
PK sampling[i]				X	X	
Clinic visit	X	X	X	X	X	X
Study drug dispensation[j]	X	X	X	X		
Study drug count	X	X	X	X	X	
Concomitant medications[k]	*Continuous from signing the ICF through the safety follow-up visit*					
Concomitant treatments and procedures	*Continuous from signing the ICF through the safety follow-up visit*					
Adverse event monitoring	*Continuous from signing the ICF through the safety follow-up visit*					

Abbreviations: BMI, body mass index; ECG, electrocardiogram; ET, early termination; ICF, informed consent form; MRI, magnetic resonance imaging; MSK, musculoskeletal; OLE, open-label extension; PK, pharmacokinetic(s).

[a] If a subject prematurely discontinues study treatment during the OLE, they will be encouraged to remain in the study and continue with all other aspects of the study. If a subject decides to prematurely discontinue study treatment during the OLE and not continue with all other aspects of the study, they will be considered to have withdrawn from the study. If a subject withdraws from the study during the OLE, they will be asked to complete the ET visit as soon as possible after the decision to terminate study participation and to complete the safety follow-up visit 7 (±3) days after their last dose of study drug. If the ET visit will be scheduled more than 7 days after the last dose of study drug, the safety follow-up and ET visits may be combined, with no duplication of assessments required.

[b] Scheduled visits may be split over 2 days if required, with a maximum of 5 business days in between visits. Unscheduled visits may be performed if clinically indicated. Subjects can travel for MRI or muscle biopsy if needed, but the use of a study-approved MRI scanner should be consistent during the trial.

[c] Weight and height will be measured and BMI will be calculated once a year (ie, Week 72, Week 120, Week 168, Week 216, etc.). Weight and height will be measured with shoes off and preferably with the same balance.

[d] [redacted]

[e] Urine pregnancy tests will be performed for all female subjects of child-bearing potential before dispensation of study drug. If pregnancy is found, subjects must be terminated from the study effective immediately.

[f] Vital signs (pulse rate, respiration rate, blood pressure, and temperature) will be collected after the subject has been seated or recumbent for at least 5 minutes and before any 12-lead ECG assessment or blood sampling is performed.

[g] Physical examination at the safety follow-up visit includes an evaluation of body systems, including but not limited to the following: skin; head, eyes, ears, nose, and throat; respiratory system; cardiovascular system; abdomen (liver, spleen); lymph nodes; neurological system; and MSK system. Symptom-directed physical examinations can occur at any time during the study if triggered by adverse events or if deemed necessary by the investigator.

[h] Twelve-lead ECGs will be performed after subjects have been recumbent for at least 5 minutes. Twelve-lead ECGs will be performed after the measurement of vital signs and before any procedures that may affect heart rate (eg, blood sampling).

[i] Blood samples for PK will be collected after dosing at the Week 144 clinic visit only, preferably ≥1 hour after dosing.

[j] The appropriate amount of study drug supply (losmapimod) will be given to the subject at each applicable visit to allow for dosing until their next scheduled study visit plus additional tablets to cover the visit window or additional study drug will be provided to the subject via a courier, as applicable. Study drug (losmapimod) will be taken twice daily and should be taken with food.

[k] All medications taken within 28 days before screening through the safety follow-up visit will be recorded.

14.4. List of Planned Summary Tables

TLF Number	Title	Analysis Set	U/R	Section	Efficacy/ Safety/ Standard	SRC
14.1.1	Table 14.1.1 Subject Disposition Open-label Analysis Set	Open-label Analysis Set	U	5.1	Standard	Y
14.1.2.1	Table 14.1.2.1 Significant Protocol Deviations through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	5.2	Standard	Y
14.1.2.2	Table 14.1.2.2 Significant Protocol Deviations During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	5.2	Standard	Y
14.1.2.3	Table 14.1.2.3 Significant Protocol Deviations During Placebo-Controlled Treatment Open-label Analysis Set	Open-label Analysis Set	R	5.2	Standard	
14.1.3	Table 14.1.3 Demographics Open-label Analysis Set	Open-label Analysis Set	U	6.1	Standard	Y
14.1.4	Table 14.1.4 Baseline Disease Characteristics Open-label Analysis Set	Open-label Analysis Set	U	6.2	Standard	
14.1.5.1	Table 14.1.5.1 Concomitant Medications through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.1	Standard	
14.1.5.2	Table 14.1.5.2 Concomitant Medications During Open-Label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	7.1	Standard	
14.1.5.3	Table 14.1.5.3 Concomitant Medications During Placebo-Controlled Treatment Open-label Analysis Set	Open-label Analysis Set	R	7.1	Standard	
14.1.6.1	Table 14.1.6.1 Treatment Duration During Losmapimod Exposure through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.2.1	Standard	
14.1.6.2	Table 14.1.6.2 Treatment Compliance During Losmapimod Exposure through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.2.2	Standard	
14.2.1	Table 14.2.1 Summary of Losmapimod Concentrations by Scheduled Time and Specimen through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	10	Efficacy	
14.2.3.1.1.1	Table 14.2.3.1.1.1 Change from Baseline in Longitudinal Composite Muscle Fat Fraction (MFF) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.1.1.4	Table 14.2.3.1.1.4 Change from Baseline in Longitudinal Composite Muscle Fat Fraction (MFF) through Data-Cut Date (ddmmmyyyy) by Sex Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.1.1.11	Table 14.2.3.1.1.11 Change from Baseline in Longitudinal Composite Muscle Fat Fraction (MFF) through Data-Cut Date (ddmmmyyyy) by Age (< 50 years old and >= 50 years old) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.1.2	Table 14.2.3.1.2 Change from Baseline in Muscle Fat Fraction (MFF) through Data-Cut Date (ddmmmyyyy) by Individual Muscles Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	

14.2.3.1.3	Table 14.2.3.1.3 Correlation Between Muscle Fat Fraction Cross-sectional Results and FSHD TUG, Classic TUG, and RWS Results through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.1.4.1	Table 14.2.3.1.4.1 Annualized Change in Longitudinal Composite Muscle Fat Fraction (MFF) through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.1.4.2	Table 14.2.3.1.4.2 Annualized Change in Longitudinal Composite Muscle Fat Fraction (MFF) in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.1.4.3	Table 14.2.3.1.4.3 Annualized Change in Longitudinal Composite Muscle Fat Fraction (MFF) in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.1.5.1	Table 14.2.3.1.5.1 Annualized Change in Muscle Fat Fraction (MFF) by Individual Muscles through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.1.5.2	Table 14.2.3.1.5.2 Annualized Change in Muscle Fat Fraction (MFF) by Individual Muscles in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.1.5.3	Table 14.2.3.1.5.3 Annualized Change in Muscle Fat Fraction (MFF) by Individual Muscles in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.2.1.1	Table 14.2.3.2.1.1 Change from Baseline in Longitudinal Composite Lean Muscle Volume (LMV) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.2.1.4	Table 14.2.3.2.1.4 Change from Baseline in Longitudinal Composite Lean Muscle Volume (LMV) through Data-Cut Date (ddmmmyyyy) by Sex Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.2.1.11	Table 14.2.3.2.1.11 Change from Baseline in Longitudinal Composite Lean Muscle Volume (LMV) through Data-Cut Date (ddmmmyyyy) by Age (< 50 years old and >= 50 years old) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.2.2	Table 14.2.3.2.2 Change from Baseline in Lean Muscle Volume (LMV) through Data-Cut Date (ddmmmyyyy) by Individual Muscles Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.2.3	Table 14.2.3.1.3 Correlation Between Lean Muscle Volume Cross-sectional Results and FSHD TUG, Classic TUG, and RWS Results through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.2.4.1	Table 14.2.3.2.4.1 Annualized Change in Longitudinal Composite Lean Muscle Volume (LMV) through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.2.4.2	Table 14.2.3.2.4.2 Annualized Change in Longitudinal Composite Lean Muscle Volume (LMV) in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.2.4.3	Table 14.2.3.2.4.3 Annualized Change in Longitudinal Composite Lean Muscle Volume (LMV) in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.2.5.1	Table 14.2.3.2.5.1 Annualized Change in Lean Muscle Volume (LMV) by Individual Muscles through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.2.5.2	Table 14.2.3.2.5.2 Annualized Change in Lean Muscle Volume (LMV) by Individual Muscles in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.2.5.3	Table 14.2.3.2.5.3 Annualized Change in Lean Muscle Volume (LMV) by Individual Muscles in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.3.1.1	Table 14.2.3.3.1.1 Change from Baseline in Longitudinal Composite Muscle Fat Infiltration (MFI) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.3.3.1.4	Table 14.2.3.3.1.4 Change from Baseline in Longitudinal Composite Muscle Fat Infiltration (MFI) through Data-Cut Date (ddmmmyyyy) by Sex Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.3.1.11	Table 14.2.3.3.1.11 Change from Baseline in Longitudinal Composite Muscle Fat Infiltration (MFI) through Data-Cut Date (ddmmmyyyy) by Age (< 50 years old and >= 50 years old) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	

14.2.3.3.2	Table 14.2.3.3.2 Change from Baseline in Muscle Fat Infiltration (MFI) through Data-Cut Date (ddmmmyyyy) by Individual Muscles Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.3.3	Table 14.2.3.1.3 Correlation Between Muscle Fat Infiltration Cross-sectional Results and FSHD TUG, Classic TUG, and RWS Results through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.3.4.1	Table 14.2.3.3.4.1 Annualized Change in Longitudinal Composite Muscle Fat Infiltration (MFI) through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.3.4.2	Table 14.2.3.3.4.2 Annualized Change in Longitudinal Composite Muscle Fat Infiltration (MFI) in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.3.4.3	Table 14.2.3.3.4.3 Annualized Change in Longitudinal Composite Muscle Fat Infiltration (MFI) in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.3.5.1	Table 14.2.3.3.5.1 Annualized Change in Muscle Fat Infiltration (MFI) by Individual Muscles through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.3.3.5.2	Table 14.2.3.3.5.2 Annualized Change in Muscle Fat Infiltration (MFI) by Individual Muscles in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.3.3.5.3	Table 14.2.3.3.5.3 Annualized Change in Muscle Fat Infiltration (MFI) by Individual Muscles in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.1.1.1	Table 14.2.4.1.1.1 Change from Baseline in Reachable Work Space (RWS) Relative Surface Area (RSA) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.1	Efficacy	
14.2.4.1.1.3.1	Table 14.2.4.1.1.3.1 Annualized Change in Reachable Work Space (RWS) Relative Surface Area (RSA) through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.1	Efficacy	
14.2.4.1.1.3.2	Table 14.2.4.1.1.3.2 Annualized Change in Reachable Work Space (RWS) Relative Surface Area (RSA) in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.1.1.3.3	Table 14.2.4.1.1.3.3 Annualized Change in Reachable Work Space (RWS) Relative Surface Area (RSA) in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	

14.2.4.2.1.1	Table 14.2.4.2.1.1 Change from Baseline in Classic Timed Up and Go (TUG) Average Completion Time (sec) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.2	Efficacy	
14.2.4.2.2.1	Table 14.2.4.2.2.1 Change from Baseline in FSHD Timed Up and Go (TUG) Average Total Completion Time (sec) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.2	Efficacy	
14.2.4.2.3	Table 14.2.4.2.3 Change from Baseline in FSHD Timed Up and Go (TUG) Average Completion Time (sec) by Segment through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.2	Efficacy	
14.2.4.2.4.1	Table 14.2.4.2.4.1 Annualized Change in Classic Timed Up and Go (TUG) Average Completion Time (sec) through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.2.4.2	Table 14.2.4.2.4.2 Annualized Change in Classic Timed Up and Go (TUG) Average Completion Time (sec) in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.2.4.3	Table 14.2.4.2.4.3 Annualized Change in Classic Timed Up and Go (TUG) Average Completion Time (sec) in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.3.1	Table 14.2.4.3.1 Change from Baseline in Total Average Dynamometry Result: All Muscles Combined, Upper Extremity, Lower Extremity through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.3	Efficacy	
14.2.4.3.2	Table 14.2.4.3.2 Change from Baseline in Average Dynamometry Result through Data-Cut Date (ddmmmyyyy) by Hand Dominance Open-label Analysis Set	Open-label Analysis Set	R	8.2.3	Efficacy	
14.2.4.3.3	Table 14.2.4.3.3 Change from Baseline in Maximum Dynamometry Result through Data-Cut Date (ddmmmyyyy) by Hand Dominance Open-label Analysis Set	Open-label Analysis Set	R	8.2.3	Efficacy	

14.2.4.3.4.1	Table 14.2.4.3.4.1 Annualized Change in Dynamometry Results through RCT+OLE Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.3	Efficacy	
14.2.4.3.4.2	Table 14.2.4.3.4.2 Annualized Change in Dynamometry Results in RCT Period Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.3.4.3	Table 14.2.4.3.4.3 Annualized Change in Dynamometry Results in OLE Period through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.4.1	Table 14.2.4.4.1 Shift in Motor Function Measure (MFM) Individual Component Score through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.4	Efficacy	
14.2.4.4.2	Table 14.2.4.4.2 Change from Baseline in Motor Function Measure (MFM) Domain 1 Score through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.4	Efficacy	
14.2.4.4.3	Table 14.2.4.4.3 Shift in Motor Function Measure (MFM) Domain 1 Score through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.4	Efficacy	
14.2.4.5	Table 14.2.4.5 Change from Baseline in FSHD Heath Index (FSHD-HI) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.5	Efficacy	
14.2.4.6.1	Table 14.2.4.6.1 Patients' Global Impression of Change (PGIC) Improved and Not Improved through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.6	Efficacy	
14.2.4.6.2	Table 14.2.4.6.2 Patients' Global Impression of Change (PGIC) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.6	Efficacy	

14.2.4.6.3	Table 14.2.4.6.3 Summary of Patients' Global Impression of Change (PGIC) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2.6	Efficacy	
14.2.4.6.4	Table 14.2.4.6.4 Patients' Global Impression of Change (PGIC) Not Worsened and Worsened through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.2.6	Efficacy	
[redacted]						
14.3.1.1.1	Table 14.3.1.1.1 Overall Treatment-Emergent Adverse Events through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1	Safety	Y
14.3.1.1.2	Table 14.3.1.1.2 Overall Treatment-Emergent Adverse Events During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1	Safety	Y
14.3.1.1.3	Table 14.3.1.1.3 Overall Treatment-Emergent Adverse Events During the Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	U	9.1	Safety	
14.3.1.2.1	Table 14.3.1.2.1 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.1	Safety	Y
14.3.1.2.2	Table 14.3.1.2.2 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term During Open-Label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.1	Safety	Y

14.3.1.2.3	Table 14.3.1.2.3 Treatment-Emergent Adverse Events by System Organ Class and Preferred Term During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	U	9.1.1	Safety	
14.3.1.3.1	Table 14.3.1.3.1 Treatment-Emergent Adverse Events by Relationship to Study Drug through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.2	Safety	Y
14.3.1.3.2	Table 14.3.1.3.2 Treatment-Emergent Adverse Events by Relationship to Study Drug During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.2	Safety	Y
14.3.1.3.3	Table 14.3.1.3.3 Treatment-Emergent Adverse Events by Relationship to Study During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	U	9.1.2	Safety	
14.3.1.4.1	Table 14.3.1.4.1 Treatment-Emergent Adverse Events by Maximum Severity through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.3	Safety	Y
14.3.1.4.2	Table 14.3.1.4.2 Treatment-Emergent Adverse Events by Maximum Severity During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1.3	Safety	Y
14.3.1.4.3	Table 14.3.1.4.3 Treatment-Emergent Adverse Events by Maximum Severity During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	U	9.1.3	Safety	
14.3.1.5.1	Table 14.3.1.5.1 Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.5	Safety	
14.3.1.5.2	Table 14.3.1.5.2 Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.5	Safety	

14.3.1.5.3	Table 14.3.1.5.3 Treatment-Emergent Adverse Events Leading to Treatment Discontinuation by System Organ Class and Preferred Term During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	R	9.1.5	Safety	
14.3.1.6.1	Table 14.3.1.6.1 Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.6	Safety	
14.3.1.6.2	Table 14.3.1.6.2 Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.6	Safety	
14.3.1.6.3	Table 14.3.1.6.3 Treatment-Emergent Adverse Events Leading to Study Withdrawal by System Organ Class and Preferred Term During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	R	9.1.6	Safety	
14.3.2.1.1	Table 14.3.2.1.1 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.4	Safety	Y
14.3.2.1.2	Table 14.3.2.1.2 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term During Open-label Extension through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.4	Safety	Y
14.3.2.1.3	Table 14.3.2.1.3 Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term During Placebo-Controlled Treatment Period Open-label Analysis Set	Open-label Analysis Set	R	9.1.4	Safety	
14.3.2.2.1	Table 14.3.2.2.1 Adverse Events Leading to Death by System Organ Class and Preferred Term through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1.7	Safety	
14.3.4.1.1	Table 14.3.4.1.1 Change from Baseline in Hematology through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.2.1	Safety	Y

14.3.4.1.2	Table 14.3.4.1.2 Shift from Baseline in Hematology through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.2.1	Safety	Y
14.3.4.2.1	Table 14.3.4.2.1 Change from Baseline in Chemistry through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.2.2	Safety	Y
14.3.4.2.2	Table 14.3.4.2.2 Shift from Baseline in Chemistry through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.2.2	Safety	Y
14.3.4.2.3	Table 14.3.4.2.3 Summary of Separate Clinically Notable Laboratory Results through Data-Cut Date (ddmmmyyyy) by Visit – Chemistry (Liver) Open-label Analysis Set	Open-label Analysis Set	U	9.2.2	Safety	Y
14.3.4.2.4	Table 14.3.4.2.4 Evaluation of Potential Drug-Induced Liver Injury (DILI) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	U	9.2.2	Safety	Y
14.3.4.4	Table 14.3.4.4 Change from Baseline in Urinalysis through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.2.3	Safety	Y
14.3.5.1	Table 14.3.5.1 Change from Baseline in Vital Signs through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.3	Safety	Y
14.3.5.2.1	Table 14.3.5.2.1 Physical Examination through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.4	Safety	Y
14.3.5.3.1	Table 14.3.5.3.1 Change from Baseline in Electrocardiogram Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.5	Safety	

14.3.5.3.2	Table 14.3.5.3.2 Electrocardiogram Interpretation by Visit through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.5	Safety	
14.3.5.3.3	Table 14.3.5.3.3 Summary of QTcF Values through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.5	Safety	

14.5. List of Planned Listings

TLF Number	Title	Analysis Set	U/R	Section	Efficacy/ Safety/ Standard	SRC
16.2.1	Listing 16.2.1 Subject Disposition Open-label Analysis Set	Open-label Analysis Set	U	5.1	Standard	Y
16.2.2	Listing 16.2.2 Protocol Deviations through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	5.2	Standard	
16.2.4.1	Listing 16.2.3.1 Demographics and Baseline Disease Characteristics Open-label Analysis Set	Open-label Analysis Set	U	6.1	Standard	Y
[redacted]						
16.2.4.3	Listing 16.2.3.3 Concomitant Medications through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.1	Standard	
16.2.4.4	Listing 16.2.3.4 Physical Examination through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.4	Safety	Y
16.2.5.1	Listing 16.2.4.1 Study Drug Accountability through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.2.1	Standard	

16.2.5.2	Listing 16.2.4.2 Study Drug Administration through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	7.2.2	Standard	
16.2.5.3	Listing 16.2.4.3 Individual Losmapimod Concentration through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	10	Efficacy	
16.2.6.1.1	Listing 16.2.6.1.1 Muscle Fat Fraction, Lean Muscle Volume and Muscle Fat Infiltration Longitudinal Scores through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2	Efficacy	
16.2.6.1.2	Listing 16.2.6.1.2 Muscle Fat Fraction, Lean Muscle Volume and Muscle Fat Infiltration Cross-sectional Scores through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.2	Efficacy	
16.2.6.2.1	Listing 16.2.6.2.1 Reachable Work Space through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.1	Efficacy	
16.2.6.2.2.1	Listing 16.2.6.2.2.1 Classic Timed Up and Go (TUG) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.2	Efficacy	
16.2.6.2.2.2	Listing 16.2.6.2.2.2 FSHD Timed Up and Go (TUG) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.2	Efficacy	
16.2.6.2.3	Listing 16.2.6.2.3 Muscle Strength (kg) by Handheld Quantitative Dynamometry through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.3	Efficacy	
16.2.6.2.4	Listing 16.2.6.2.4 Motor Function Measure (MFM) Domain 1 Score through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.4	Efficacy	

16.2.6.2.5	Listing 16.2.6.2.5 Facioscapulohumeral Muscular Dystrophy Health Index (FSHD-HI) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.5	Efficacy	
16.2.6.2.6	Listing 16.2.6.2.6 Patient Global Impression of Change (PGIC) through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.3.6	Efficacy	
16.2.7.1	Listing 16.2.7.1 Adverse Events through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.1	Safety	Y
16.2.7.2	Listing 16.2.7.2 Serious Adverse Events through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1	Safety	Y
16.2.7.3	Listing 16.2.7.3 Adverse Events Leading to Treatment Discontinuation through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1	Safety	
16.2.7.4	Listing 16.2.7.4 Adverse Events Leading to Study Withdrawal through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1	Safety	
16.2.7.5	Listing 16.2.7.5 Deaths through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.1	Safety	
16.2.8.1	Listing 16.2.8.1 Laboratory Results through Data-Cut Date (ddmmmyyyy)- Hematology Open-label Analysis Set	Open-label Analysis Set	U	9.2.1	Safety	Y
16.2.8.2.1	Listing 16.2.8.2.1 Laboratory Results through Data-Cut Date (ddmmmyyyy) - Chemistry Open-label Analysis Set	Open-label Analysis Set	R	9.2.2	Safety	Y

16.2.8.2.2	Listing 16.2.8.2.2 Laboratory Results of Subjects with Drug-induced Liver Injury through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	9.2.2	Safety	
16.2.8.3	Listing 16.2.8.3 Laboratory Results through Data-Cut Date (ddmmmyyyy) - Urinalysis Open-label Analysis Set	Open-label Analysis Set	R	9.2.3	Safety	Y
16.2.8.4	Listing 16.2.8.4 Laboratory Results through Data-Cut Date (ddmmmyyyy) - Coagulation Open-label Analysis Set	Open-label Analysis Set	R	9.2.4	Safety	
16.2.8.5	Listing 16.2.8.5 Vital Sign Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.3	Safety	Y
16.2.8.6	Listing 16.2.8.6 Electrocardiogram Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	9.5	Safety	Y

14.6. List of Planned Figures

TLF Number	Title	Analysis Set	U/R	Section	Efficacy/ Safety/ Standard	SRC
14.2.1	Figure 14.2.1 Mean (+/- SE) Losmapimod Concentrations through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	U	10	Efficacy	
14.2.2.1	Figure 14.2.2.1 Mean (+/- SE) Change from Baseline in Longitudinal Composite Muscle Fat Fraction (MFF) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	8.2	Efficacy	
14.2.2.2	Figure 14.2.2.2 Mean (+/- SE) Change from Baseline in Longitudinal Composite Lean Muscle Volume (LMV) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	8.2	Efficacy	
14.2.2.3	Figure 14.2.2.3 Mean (+/- SE) Change from Baseline in Longitudinal Composite Muscle Fat Infiltration (MFI) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	8.2	Efficacy	
14.2.3.1	Figure 14.2.3.1 Mean (+/- SE) Change from Baseline in Reachable Work Space (RWS) Relative Surface Area (RSA) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.4.1	Figure 14.2.4.1 Mean (+/- SE) Change from Baseline in Classic Timed Up and Go (TUG) Average Completion Time (sec) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.5.1	Figure 14.2.5.1 Mean (+/- SE) Change from Baseline in Total Average Dynamometry through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	

14.2.5.2	Figure 14.2.5.2 Mean (+/- SE) Change from Baseline in Average Dynamometry by Hand Dominance through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.5.3	Figure 14.2.5.3 Mean (+/- SE) Change from Baseline in Maximum Dynamometry by Hand Dominance through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.6.1	Figure 14.2.6.1 Mean (+/- SE) in Patient Global Impression of Change (PGIC) through Data-Cut Date (ddmmmyyyy) by Visit Open-label Analysis Set	Open-label Analysis Set	R	OLE	Efficacy	
14.2.7.1	Figure 14.3.1 Scatterplot of Muscle Fat Fraction Cross-sectional Results and FSHD TUG, Classic TUG and RWS Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	U	8.1	Efficacy	
14.2.7.2	Figure 14.3.2 Scatterplot of Lean Muscle Volume Cross-sectional Results and FSHD TUG, Classic TUG and RWS Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	
14.2.7.3	Figure 14.3.3 Scatterplot of Muscle Fat Infiltration Cross-sectional Results and FSHD TUG, Classic TUG and RWS Results through Data-Cut Date (ddmmmyyyy) Open-label Analysis Set	Open-label Analysis Set	R	8.1	Efficacy	