16.1.9 Documentation of Statistical Methods

MRT5005-101 Final Statistical Analysis Plan, Version 1.0, 26 October 2021

STATISTICAL ANALYSIS PLAN
26 October 2021 FINAL v1.0

A Phase 1/2, Randomized, Double-Blind, Placebo-Controlled, Combined Single and Multiple Ascending Dose Study Evaluating the Safety, Tolerability, and Biological Activity of MRT5005 ([redacted] mRNA[redacted] LNP) Administered by Nebulization to Adult Subjects with Cystic Fibrosis

PROTOCOL NUMBER MRT5005-101
Version 5.0, Amendment 4

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LIST OF ABBREVIATIONS

AE	adverse event
BMI	body mass index
CF	cystic fibrosis
CFQ-R	cystic fibrosis questionnaire-revised
CFTR	cystic fibrosis transmembrane conductance regulator
[redacted]	[redacted]
CSR	clinical study report
ECG	electrocardiogram
FEF	forced expiratory flow
FEV_1	forced expiratory volume in 1 second
hCFTR	human cystic fibrosis transmembrane conductance regulator
[redacted]	
ICH	International Council for Harmonisation
MAD	multiple ascending dose
MedDRA	Medical Dictionary for Regulatory Activities
PEF	peak expiratory flow
PSRC	Protocol Safety Review Committee
qPCR	quantitative polymerase chain reaction
SAD	single ascending dose
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SUSAR	suspected unexpected serious adverse reaction
TEAE	treatment-emergent adverse event
ULN	upper limit of normal

1. PURPOSE OF THE ANALYSES

The statistical analysis plan (SAP) is being developed after review of the Translate Bio, Inc., protocol number MRT5005-101, but before the final analyses of the data. The SAP contains detailed information to aid in the implementation of the statistical analyses and reporting of the study data for use in the clinical study report (CSR).

This SAP is being written with due consideration of the recommendations outlined in the most recent International Council for Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

This SAP describes the analysis sets that will be analyzed, the subject characteristics parameters, and the safety parameters that will be evaluated. The details of the specific statistical methods that will be used are provided in the SAP. Table, figure, and listing specifications are provided in separate documents.

2. PROTOCOL SUMMARY

2.1 Study Objectives

2.1.1 Primary Objective

To evaluate the safety and tolerability of single and multiple escalating doses of MRT5005 administered by nebulization to adult subjects with cystic fibrosis (CF).

2.1.2 Secondary Objective

To evaluate the effect on percent predicted forced expiratory volume in 1 second ($ppFEV_1$) and other spirometry parameters after single and multiple escalating doses of MRT5005 administered by nebulization to adult subjects with CF.

2.2 Study Endpoints

2.2.1 Primary Endpoint

The safety and tolerability of nebulized MRT5005 will be assessed based on the types, frequency, and severity of treatment-emergent AEs including pulmonary exacerbations; concomitant medication use; and changes from baseline in physical examination, weight, vital signs, oxygen saturation (pulse oximetry), ECG, standard clinical laboratory tests, chest x-ray, and spirometry as a measure of pulmonary function.

2.2.2 Secondary Endpoint

The biological activity of nebulized MRT5005 will be assessed based on changes from baseline in $ppFEV_1$ and other spirometry parameters.

2.3 Overall Study Design and Plan

This phase 1/2 study is designed as a randomized, double-blind, placebo-controlled, combined single and multiple ascending dose (SAD and MAD) trial, which will be conducted in 3 parts. Subjects will be administered single and multiple escalating doses of MRT5005 in Parts A and B of the study, respectively. In Part D, subjects will be administered 5 consecutive daily doses of 4 mg MRT5005 or placebo. Part C (bronchoscopy groups) was removed from the protocol in the 3rd amendment to the protocol (Version 4.0 dated 29 July 2019).

The study will be conducted at multiple centers in the United States with expertise in treating CF subjects. At least 40 adult male and female subjects with CF, 18 years of age or older, are planned to participate in the study. Subjects who are clinically stable with a forced expiratory volume in 1 second (FEV_1) $\geq$50% and $\leq$90% predicted, and who meet all inclusion criteria and none of the exclusion criteria, will be eligible for the study. The inclusion and exclusion criteria for the study are enumerated in Sections 4.1 and 4.2 of the protocol, respectively. Women of childbearing potential will also be eligible to participate if they are willing and able to comply with contraception requirements.

If subjects do not complete the study or complete certain procedures, additional subjects will be enrolled at the Sponsor's discretion to ensure that at least 16, 16, and 8 evaluable subjects complete Parts A, B, and D of the study, respectively. For Part A, an evaluable subject will be defined as a subject with 1 completed dose and 4 weeks of safety follow-up. For Part B, an evaluable subject will be defined as a subject with 4 completed doses occurring on 4 consecutive weeks with 4 weeks of safety follow-up. For Part D, an evaluable subject will be defined as a subject with 4 completed doses occurring within 5 consecutive days with 4 weeks of safety follow-up. A SAD dose group may be repeated in a new group of subjects in Part A to further assess the safety of the dose level before escalating to the next higher dose level, or before allowing it to proceed from Part A (SAD) to Part B (MAD). It is expected that no more than 1 additional group of 4 subjects will be enrolled into the study in Part A. Therefore, up to a maximum of 44 evaluable subjects may participate in the study.

Each part of the study will consist of a screening period, a treatment period, and a follow-up period. Multiple visits during the screening period, from Day -28 to Day -2 (Parts A and B) or from Day -28 to Day -1 (Part D), may be necessary for the subject to complete all of the required screening procedures and tests. During the treatment period, subjects participating in Part A will be confined to the study center from Day -1 to Day 2 and will receive a single dose of investigational product. This will be followed by a safety follow-up period, which continues up to the final study visit on Day 337. During the safety follow-up, clinic visits for Part A subjects will be performed on an outpatient basis.

No confinement will be required of subjects in Parts B and D of the study; these subjects will perform all clinic visits in the treatment and follow-up periods as outpatients. During the treatment period of Part B (Day -1 to Day 33), subjects will receive 5 doses of investigational product, administered 1 dose per week for 5 weeks. During the treatment period of Part D (Day 1 to Day 5), subjects will receive 5 doses of IP, administered 1 dose per day for 5 days. The safety follow-up period will continue up to the last study visit on Day 365 for Part B and Day 341 for Part D.

In Part A (SAD groups), 4 groups consisting of 4 subjects each will be enrolled sequentially to receive single doses of MRT5005 or placebo (normal saline) administered by nebulization. Three dose levels of MRT5005 were planned to be investigated: 8, 16, and 24 mg of [redacted] mRNA [[redacted] mRNA (the active drug substance of MRT5005; nominal doses)]. An additional treatment group (20 mg) was added after blinded safety information from the 24 mg dose group revealed the occurrence of febrile reactions in 3 of 4 subjects. Within each dose group, the enrollment and treatment of the 4 subjects will be staggered by at least 1 week. Subjects will be randomized in a 3:1 ratio to receive a single dose of either MRT5005 or placebo (3 subjects to receive MRT5005 and 1 subject to receive placebo per dose group).

The protocol safety review committee (PSRC) will be responsible for reviewing safety data and, based on this review, making the decision to dose escalate from the 8 mg starting SAD dose level to the 16 mg dose level, and then to the 24 mg maximum dose level. The 20 mg dose level will be evaluated after the 24 mg dose level.

The decision to begin enrollment and treatment of the initial 8 mg multiple-dose group in Part B will also be made by the PSRC, based on a review of at least 28 days of safety follow-up for all subjects who received a single dose of the 8 mg dose level in Part A.

In Part B (MAD groups), 4 groups consisting of 4 subjects each will be enrolled sequentially to receive multiple doses of MRT5005 or placebo administered by nebulization. Three groups will be enrolled sequentially to receive dose levels of MRT5005 investigated as single doses in Part A (8, 16, and 20 mg). An additional dose level that was not investigated in Part A (12 mg) will also be evaluated in Part B. The 12 mg dose group may be enrolled in parallel with the 16 and/or 20 mg dose group. Within each dose group, subjects will be randomized in a 3:1 ratio to receive 5 doses of either MRT5005 or placebo (3 subjects to receive MRT5005 and 1 subject to receive placebo per dose group), administered 1 dose per week for 5 weeks. The enrollment and treatment of the 4 subjects within each dose group will be staggered by at least 2 weeks (the next subject in the dose group will be enrolled and treated only when the previous subject has received their second dose and at least 1 week of safety follow-up), with the exception of the 12 mg dose group in Part B which may not require staggered treatment as outlined in Protocol Section 3.1.

Similar to Part A, the PSRC will be responsible for reviewing safety data and making the decision to dose escalate.

In Part D, 8 subjects will be randomized in a 3:1 ratio to receive 5 doses of either 4 mg MRT5005 or placebo, administered at 1 dose per day for 5 consecutive days.

Because single doses up to 20 mg, as well as 5 weekly doses up to 16 mg have been tolerated in Parts A and B, the enrollment and treatment of the 8 subjects within Part D will not be staggered.

All subjects in the study will be monitored for safety for 12 months after administration of the last dose of investigational product (post-single dose in Part A; post-fifth dose in Parts B and D). The safety and tolerability of nebulized MRT5005 will be assessed based on the types, frequency, and severity of treatment-emergent adverse events (TEAEs) reported including the number of pulmonary exacerbations; concomitant medication use; and changes from baseline in physical examination, weight, vital signs, oxygen saturation (pulse oximetry), electrocardiogram (ECG), standard clinical laboratory tests, chest x-ray, and spirometry as a measure of pulmonary function. As part of the safety evaluation, assays to detect [redacted] mRNA and [redacted] in the blood post-treatment will be performed along with assays to detect antibody and T cell immune responses to CFTR protein and anti-PEG (polyethylene glycol) antibodies.

This will be conducted as a double-blind study, except for the last part of the 12-month follow-up. All subjects in the study will be followed up for 12 months after their last dose, but the treatment randomization for the 8, 16, and 24 mg single dose groups will be unblinded 1 month after the last dose of the last subject in the 24 mg single dose group in Part A. The blind will be maintained in the 20 mg single dose group in Part A, as well as the 8, 16, and 12 mg multiple dose groups in Part B until the 1-month time point after the last dose (Day 57) of

the last subject dosed in the 12 mg dose group. For the 20 mg multiple dose group in Part B, the blind will be maintained until the last subject in this group has reached the 1-month time point after the last dose day (Day 57). For Part D, the blind will be maintained until the 1-month time point after the last dose (Day 32) of the last subject in Part D.

During the double-blind period, the investigators and all study staff involved in the evaluation of subject eligibility, administration of IP, and assessment of the study outcomes will be blinded to treatment assignment (MRT5005 vs. placebo within each dose group) until planned unblinding. All subjects and their families, as well as sponsor personnel in direct contact with the study center, will also be blinded.

A study flow chart is presented in Appendix 17.1, and a flow diagram of subject enrollment and treatment allocation is presented in Appendix 17.2. Table 1 through Table 9 in the protocol present the schedule of study procedures to be performed during each the 3 periods in Part A, B, and D of the study.

2.4 Treatment Regimens and Randomization

In all three parts of the study, subjects will be randomized to receive either MRT5005 or placebo (normal saline) in a 3:1 ratio. Subjects will receive a single dose in Part A, 5 weekly doses in Part B, and 5 consecutive daily doses in Part D. The 8 mg dose level of MRT5005 will be the SAD starting dose in Part A followed by sequential escalation to the 16 mg and 24 mg dose levels of MRT5005. An additional 20 mg treatment group was added to Part A after blinded safety information from the 24 mg group revealed the occurrence of febrile reactions in 3 of 4 subjects. The 8 mg dose level of MRT5005 will be the MAD starting dose in Part B, followed by sequential escalation to the 16 mg and 20 mg dose levels of MRT5005. An additional 12 mg group was added to Part B to explore the safety profile at an intermediate dose level that was not investigated as a single dose in Part A. The 12 mg dose level may begin enrollment in parallel with the 16 mg dose level. The enrollment and treatment of the 4 subjects within each MAD dose group will be staggered by at least 2 weeks (the next subject in the dose group will only be enrolled and treated when the previous subject has received their second dose and there is approximately 1 week of safety follow-up), with the exception of the 12 mg dose group in Part B which may not require staggered treatment. In Part D, 8 subjects will be randomized in a 3:1 ratio to receive 5 doses of either 4 mg MRT5005 or placebo, administered at 1 dose per day for 5 consecutive days. Because single doses up to 20 mg, as well as 5 weekly doses up to 16 mg have been tolerated in Parts A and B, the enrollment and treatment of the 8 subjects within Part D will not be staggered. During the treatment of subjects in Part D, should AEs occur that indicate the study drug is not tolerated well, the enrollment and treatment of subjects may be terminated by the PSRC and Sponsor, and enrollment and treatment of a lower dose strength may be considered in the remaining subjects in the cohort. For example, if the tolerability of the 4 mg daily dose level is found to be unacceptable, then the 2 mg dose level can be considered for investigation. Subjects will not be allowed to participate in more than 1 part of the study.

2.5 Sample Size Determination

The sample size is not based on any statistical considerations. Instead, the sample size is based on traditional phase 1 first-in-human study designs for this disease population. In Parts A and B of the study, the inclusion of 4 subjects per dose group (3 subjects randomized to MRT5005 and 1 subject randomized to placebo) will provide basic information on safety and tolerability during dose escalation of MRT5005. In Part D, 8 subjects treated at 4 mg MRT5005 or placebo (6 subjects randomized to MRT5005 and 2 subjects randomized to placebo) will provide further safety and tolerability data on MRT5005. This study is also designed with the flexibility to enroll additional groups of subjects to support meeting its objectives.

2.6 Protocol Safety Review Committee

The PSRC will conduct a safety data review before each dose-escalation in Parts A and B and before the initiation of enrollment and treatment of subjects in the first MAD group in Part B. Based on these safety data reviews, the PSRC will decide whether or not to proceed at each of these time points in the study, per Protocol Sections 3.4.1 and 3.4.2.

Based on the judgment of the PSRC:

- A Part A dose group may be repeated in a new group of subjects to further assess the safety of the dose level before escalating to the next higher dose level or before multiple dosing is allowed to proceed in Part B.

The PSRC will be notified of all serious adverse events deemed possibly, probably, or definitely related to investigational product (including suspected unexpected serious adverse reaction [SUSAR]) reports in real-time. The PSRC will be notified of 2 occurrences of significant febrile reactions in different participants (defined as ≥ Grade 2 fever [>39.0°C] associated with systemic symptomatology [eg, body aches, malaise, nausea]) within 24 hours following administration of IP. If an adverse event of special interest (AESI), as defined in Protocol Section 8.1.8, is reported during the study, the PSRC will be notified by the Sponsor in real-time. The PSRC will receive SAE listings following each dose group and may choose to receive more frequent SAEs listings at any time during the study. The PSRC will also review all available and relevant safety data if stopping criteria are met during the study to determine whether the study will continue or be terminated. The PSRC charter includes the roles and responsibilities of the PSRC, format and structure of PSRC meetings, and details the study stopping criteria.

2.7 Dose Group and Study Stopping Criteria and Unblinding

Investigational product administration will be halted for all subjects in a dose group, as well as any subjects in an ongoing higher dose group if any of the following stopping criteria are met:

a. Two subjects in a dose group experience a significant febrile reaction (defined as ≥ Grade 2 fever [>39.0°C] associated with systemic symptomatology [eg, body aches, malaise, nausea]) within 24 hours following administration of IP.
b. Two subjects in a dose group experience a suspected moderate to severe allergic/hypersensitivity reaction, including but not limited to anaphylaxis, generalized rash, edema or bronchospasm possibly related to drug treatment.

Investigational product administration will be halted for all subjects in Part D if the following stopping criterion is met:

a. Three subjects experience Grade 1 fevers (38.0 to 39.0 °C) associated with systemic symptomatology (eg, body aches, malaise, nausea) onset within 24 hours following administration of IP on ≥3 separate occasions.

Investigational product administration will be halted for all subjects if any of the following stopping criteria are met:

a. A subject experiences a Grade 4, life-threatening treatment-emergent AE or death that is considered probably or definitely related to investigational product by the Investigator.
b. Two or more subjects in a dose group experience 1 or more moderate or severe pulmonary exacerbations during the 5-week treatment period in part B or through Day 11 (1 week post-5th dose) in Part D.
c. Two or more subjects in a dose group experience a decrease in predicted FEV1 of at least 25 % compared to the baseline value (defined as the average of the Day -1 and Day 1 pre-dose values) during the 5-week treatment period in Part B or through Day 11 (1 week post-5th dose) in Part D that cannot be explained, in the opinion of the PI, by the underlying disease of CF and that is confirmed on 2 separate occasions at least 3 days apart.
d. Two or more subjects in the study experience a suspected serious allergic/hypersensitivity reaction, including but not limited to anaphylaxis, generalized rash or bronchospasm likely to be related to drug treatment.
e. Two or more subjects in a dose group experience a deterioration in liver function, as detailed below:
    i. Elevation of ALT or AST to >5x ULN in a subject regardless of baseline value
    ii. Elevation of ALT or AST to >3x ULN in a subject with a normal baseline or elevation of >3x ULN from the subject's actual baseline if not normal, with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (>5%).
    iii. Elevation of ALT or AST to >3x ULN in a subject with a normal baseline or elevation of >3x ULN from the subject's actual baseline if not normal, and total bilirubin >2x ULN or INR >1.5.

To determine whether these stopping rules have been met, the relevant data will be reviewed by the PSRC. To ensure subject safety, the PSRC may request unblinding the treatment assignment(s) for an individual subject or for an entire dose group.

3. GENERAL ANALYSIS AND REPORTING CONVENTIONS

The following is a list of general analysis and reporting conventions to be applied for this study. Where appropriate, clarification is provided throughout this SAP to document planned differences for analyses by study part.

Categorical variables will be summarized using counts (n) and percentages (%) and will be presented in the form "n (xx.x)." If a count is 0, 0% will be shown for the percentage. To ensure completeness, summaries for categorical and discrete variables will include all categories, even if no subjects had a response in a particular category.

Continuous variables will be summarized using number of subjects (n), value for each subject, mean, and SD. The mean will be reported to 1 more level of precision than the original observations, and the SD will be reported to 2 more levels of precision than the original observations, up to a maximum of 4 decimal places.

All analyses will be performed using SAS® System version 9.4 or later.

Dates in listings will be displayed as yyyy-mm-dd (e.g., 2015-01-24).

In general, age will be calculated in years using the date of birth and the date of informed consent as [(date of informed consent – date of birth)]/365.25, rounded down to the next largest integer using the floor function.

Unless otherwise specified, the baseline value for all measures is the last non-missing value prior to the first dose, obtained on or before the date of the first dose of study drug. For measurements that occur on the date of the first dose of study drug with time collected, the measurement will be considered the baseline value if the measurement time is prior to the time of the first dose. The average of the results from the testing on Day -1 and at pre-dose on Day 1 will serve as the subject's baseline for spirometry testing for Part A and Part B. For Part D, the Day 1 pre-dose result will serve as the subject's baseline for spirometry testing. The ECG collected on Day -1 will serve as the subject's baseline ECG for Part A and Part B. For Part D, the screening ECG will serve as the subject's baseline ECG.

For any laboratory values containing an inequality in the result, the numeric portion of the result will be used for analysis (e.g., <0.1 will be treated as 0.1).

Unless otherwise specified, each display will be presented separately for each study part. For any by study part displays categorized by dose group, summaries will show columns for the 4 mg dose group, 8 mg dose group, 12 mg dose group, 16 mg dose group, 20 mg dose group, 24 mg dose group, and a pooled placebo group, as applicable for each study part. A total column will be displayed where applicable.

Where possible and when specified, integrated displays will be presented combining data from all study parts by treatment (all active MRT5005 treatment dose groups combined, all pooled placebo groups combined).

For any by study part displays categorized by dose group, summaries will show columns for the 4 mg dose group, 8 mg dose group, 12 mg dose group, 16 mg dose group, 20 mg dose group, 24 mg dose group, and a pooled placebo group, as applicable for each study part. A total column will be displayed where applicable.

All data listings and figures will be presented by study part, unless otherwise specified.

4. ANALYSIS SETS

4.1 Safety Analysis Set

The primary analysis population for safety will be the safety analysis set, which will include all randomized subjects who received investigational product. For all safety analyses, subjects will be analyzed according to the treatment they actually received.

5. STUDY PATIENTS

5.1 Disposition of Patients

The disposition of subjects will be summarized for all subjects screened in the study. The following disposition information will be summarized overall for each study part, and for the study overall:

- The number and percentage of subjects that were screened, randomized, that were screen failures, and the reason for screen failure

The following disposition information will be summarized for the safety analysis set for each study part by dose group, and for the study overall by pooled treatment group:

- The number and percentage of subjects who completed the study
- The number and percentage of subjects who discontinued the study and the reason for premature discontinuation

A data listing of subject disposition for all subjects in the safety analysis set and a data listing of screen failures for all screened subjects will also be provided.

A data listing of visits not done, or completed as a home health visit or telephone visit as a replacement for a scheduled in-clinic visit and the corresponding reason for all subjects in the safety analysis set will be provided.

5.2 Protocol Deviations

Protocol deviations for all subjects in the safety analysis set will be summarized for each study part by type and dose group. A data listing of all protocol deviations for all subjects in the safety analysis set will also be provided.

6. DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Subject demographics and other baseline characteristics will be summarized descriptively for the safety analysis set for each study part, and for the study overall by pooled treatment group. The demographic and baseline characteristic summaries will be used to describe the study population.

Demographic data will include age, sex, race, ethnicity, baseline percent predicted FEV_1, concomitant CFTR modulator use, and genotype. Genotype will be summarized by first mutation class and second mutation class (e.g., 'Class I/Class II'). Age (years) will be calculated using the date of birth and the date of informed consent, as described in Section 3.

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 to identify the system organ class and preferred term. A summary table will be presented by dose group to reflect a count of medical history events occurring in subjects in the safety analysis set within each system organ class and preferred term for each study part, and for the study overall. All percentages will use the number of subjects in the safety analysis set as the denominator. Therefore, if a subject has more than 1 medical history event within a system organ class, the subject will be counted only once in that system organ class. If a subject has more than 1 medical history event that codes to the same preferred term, the subject will be counted only once for that preferred term. Tabular summaries will be sorted by overall (MRT5005 + Placebo) descending frequency by system organ class and by preferred term.

Individual data for demographics and medical history will be presented in the data listings for subjects in the safety analysis set.

7. MEASUREMENTS OF TREATMENT COMPLIANCE

Treatment compliance and exposure to investigational product will be summarized in terms of number of doses (total, full, and partial) administered. The number and percentage of subjects with 1, 2, 3, 4, or 5 total doses (sum of full and partial) administered will be presented by dose group for each study part, and by pooled treatment group for the study overall. The number of full doses and partial doses administered will be separately summarized continuously using descriptive statistics by dose group for each study part, and by pooled treatment group for the study overall. The number of full doses administered is the number of individual occurrences (days) for which a subject received a full dose of investigational product based on the completion of nebulization for the expected number of medication chambers, even if there was excess residual observed in the chamber after completion of nebulization. A partial dose refers to incomplete nebulization. Full and partial doses are independent of the presence or absence of excess residual in the medication chamber.

Individual data for dosing, including the start and end dates and time of nebulization along with assessments of whether nebulization was complete and whether excess residual was present in the medication chamber will be listed by visit and nebulizer for subjects in the safety analysis set. The number of full doses and partial doses administered for each subject will be presented in a data listing for subjects in the safety analysis set. The following individual data for dosing for each subject at each visit will be presented in a data listing for subjects in the safety analysis set: date of IP administration, whether full dose was administered, reason if full dose not administered, actual number of medication chambers completed, and the expected number of medication chambers completed.

8. EFFICACY EVALUATION

Not applicable.

9. SAFETY EVALUATION

9.1 Overview of Safety Analysis Methods

The safety analyses will be performed using the safety analysis set for the safety measures, which include extent of drug exposure, adverse events (AEs), vital signs, clinical laboratory data, ECGs, pulse oximetry, chest x-rays, spirometry, physical examinations, concomitant medications, and serum inflammatory markers.

Safety data will not be imputed, except for partial dates, which will be imputed only for defining TEAEs and for the calculation of the duration of the AE. Completely missing dates will not be imputed and any AE with a completely missing date will be classified as a TEAE. Imputed dates will not be presented in data listings.

Partial dates will be imputed for the purposes of defining TEAEs as follows:

- For a missing start day where the month and year are present, the start day will be set to the first day of the month, unless 1) the first day of the month is before the date of first dose of study drug and the month and year are the same as the month and year of the date of first dose of study drug, and 2) the end date is on or after the date of first dose of study drug or the end date is completely missing, in which case the start day will be set to the first day of first dose of study drug.
- For a missing start day and month where the year is present, the start day and month will be set to January 1st, unless 1) January 1st is before the date of first dose of study drug and the year is the same as the year of the date of first dose of study drug, and 2) the end date is on or after the date of first dose of study drug or the end date is completely missing, in which case the start day and month will be set to that of the date of first dose of study drug.
- For a missing end day where the month and year are present, the end day will be set to the last day of the month, unless the month and year are the same as the month and year of the last contact date for the subject, in which case the end day will be set to that of the subject's last contact date.
- For a missing end day and month where the year is present, the end day and month will be set to the subject's last contact date, unless the year of the subject's last contact date is greater than the end year, in which case the end day and month will be set to December 31st.

9.2 Extent of Exposure

Extent of exposure and treatment compliance are described in Section 7.

9.3 Adverse Events

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 to identify the system organ class and preferred term.

Treatment-emergent AEs are defined as events that are newly reported or reported to worsen in severity after the start of treatment. Adverse events that occur after the treatment start date, occur on the treatment start date with a time that is equal to or after treatment start time, or that have a missing AE start date will be categorized as treatment-emergent. Treatment-emergent AEs will be summarized for the safety analysis set.

For summaries of TEAEs by time interval, the categorizations for Part A will be: Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 29, and Study Day > 29. The categorizations for Part B will be: Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 36, 1 ≤ Study Day ≤ 57, and Study Day > 57. The categorizations for Part D will be: Overall, Study Day 1, 1 < Study Day ≤ 5, 1 ≤ Study Day ≤ 11, 1 ≤ Study Day ≤ 32, and Study Day > 32. The categorizations for the study overall will be: Overall, through 1 month post-dose (Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively), after 1 month post-dose (> Day 29, > Day 57, and > Day 32 for Part A, Part B, and Part D, respectively). Any TEAE with a completely missing start date will not be categorized into a specific time interval, but will be included in the Overall category.

Any dose limiting toxicities identified will be addressed in the clinical study report (CSR).

9.3.1 Overall Summary of AEs

An overall summary of AEs will be presented by dose group and will reflect a count of TEAEs, treatment-emergent serious adverse events (SAEs), TEAEs by relationship to investigational product, and TEAEs by severity. Additionally, the table will reflect the count and percentage of subjects experiencing the following: any TEAEs, SAEs, TEAEs leading to treatment discontinuation, TEAEs resulting in death, TEAEs classified as pulmonary exacerbations (investigator and protocol-defined), TEAEs classified by relationship to investigational product, TEAEs classified by relationship to nebulization/treatment administration, and TEAEs by severity. The overall summary of AEs will be presented for the overall time period for each study part, as well as for the study overall. The overall summary of AEs will also be presented for the overall time period and through 1 month post-dose (Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively) by pooled treatment group. All percentages will use the number of subjects in the safety analysis set as the denominator.

9.3.2 Subject-level and Event-level Summary of AEs

A summary table will be presented for each study part by dose group to reflect a count and percentage of subjects experiencing at least 1 TEAE in each system organ class and preferred term and a count of TEAEs occurring in subjects in the safety analysis set within each system organ class and preferred term. All percentages will use the number of subjects in the safety analysis set as the denominator. Therefore, if a subject has more than 1 AE within a system organ class, the subject will be counted only once in that system organ class. If a subject has more than 1 AE that codes to the same preferred term, the subject will be counted only once for that preferred term. For the event-level summaries, subjects experiencing more than 1 AE within a system organ class or preferred term will be counted more than once for that system

organ class or preferred term. Tabular summaries will be sorted by descending overall (MRT5005 + Placebo) frequency in subject counts by system organ class and by preferred term.

Using the same subject-level and event-level counting rules, a summary table of TEAEs by preferred term will be presented for the overall time period by dose group for each study part, as well as separately through Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively. In addition, the summary of AEs by preferred term will be presented for the study overall for the overall time interval and through 1 month post-dose (Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively) by pooled treatment group.

All AEs will be presented in data listings for subjects in the safety analysis set, including a flag to distinguish if the AE was treatment-emergent.

9.4 Deaths, Serious Adverse Events, and Other Significant Adverse Events

Treatment-emergent SAEs and adverse events of special interest will be summarized for all subjects in the safety analysis set for each study part by dose group and time interval. Summary tables will be presented by dose group to reflect a count and percentage of subjects experiencing at least 1 TEAE in each system organ class and preferred term (subject-level analysis) and a count of TEAEs (event-level analysis) occurring in subjects in the safety analysis set within each system organ class and preferred term within each AE subset (serious, AESIs). All percentages will use the number of subjects in the safety analysis set as the denominator. Therefore, for the subject-level analysis, if a subject has one or more AE within a system organ class, the subject will be counted only once in that system organ class. If a subject has one or more AE that codes to the same preferred term, the subject will be counted only once for that preferred term. For the event-level analysis, subjects experiencing more than 1 AE within a system organ class or preferred term will be counted according to the number of AEs they experience (more than once) for that system organ class or preferred term. Tabular summaries will be sorted by descending overall (MRT5005 + Placebo) frequency in subject counts by system organ class and by preferred term.

Using the same subject-level and event-level counting rules, treatment-emergent pulmonary exacerbations (investigator and protocol-defined) will be summarized by preferred term for all subjects in the safety analysis set for each study part by dose group and time interval.

Treatment-emergent febrile reactions and hypersensitivity reactions will be presented as a count of febrile reactions, febrile reactions by severity, hypersensitivity reactions, and hypersensitivity reactions by severity. Additionally, the table will reflect the count and percentage of subjects experiencing the following: any febrile reaction, any febrile reaction by severity, any hypersensitivity reaction, and any hypersensitivity reaction by severity. The summary will be for all subjects in the safety analysis set by dose group for each study part. In addition, the summary of treatment-emergent febrile reactions and hypersensitivity reactions will be presented for all subjects in the safety analysis set for the study overall by pooled treatment group. Febrile reactions will be identified based on a preferred term of body temperature increased or preferred term of pyrexia within the 24 hours after completion of

nebulization on any dosing day with at least one other systemic symptom reported as a preferred term of headache, arthralgia, myalgia, fatigue, chills, nausea, or vomiting within the 24 hours after completion of nebulization on any dosing day. Severity grade for febrile reactions will be based on the maximum severity of the preferred terms comprising the febrile reaction. Hypersensitivity reactions will be identified based on a preferred term of hypersensitivity within the 24 hours after completion of nebulization on any dosing day.

Adverse events leading to withdrawal from treatment, AEs resulting in death, pulmonary exacerbations (investigator and protocol-defined), adverse events of special interest, and SAEs will be presented in data listings for subjects in the safety analysis set. Adverse events of pyrexia or body temperature increased during nebulization or within the 24 hours after completion of nebulization on any dosing day will also be listed for subjects in the safety analysis set. This listing will include all adverse events that occurred during nebulization or within the 24 hours after completion of nebulization for subjects that had an adverse event of pyrexia or body temperature increased during nebulization or within the 24 hours after completion of nebulization on any dosing day. All adverse events that occurred during nebulization or within the 24 hours after completion of nebulization will also be listed for subjects in the safety analysis set. Febrile reactions and hypersensitivity reactions within the 24 hours after completion of nebulization on any dosing day will also be listed for subjects in the safety analysis set. This listing will include all adverse events that meet the specified febrile reaction or hypersensitivity criteria that occurred within the 24 hours after completion of nebulization for subjects that had a febrile reaction or hypersensitivity reaction within the 24 hours after completion of nebulization on any dosing day.

9.5 Clinical Laboratory Evaluation

Baseline and all post-baseline visit values and change from baseline to post-baseline in laboratory parameters for clinical chemistry and hematology will be summarized for the safety analysis set for each study part by dose group using descriptive statistics, as described in Section 3.

C reactive protein (mg/L), white blood cell (x10^9/L), and neutrophil (%) results for each subject at each visit by dose group for each study part will be provided in a line plot. An additional line plot of C reactive protein (mg/L) results for each subject at each visit by dose group will be provided for visits through Day 29 for Part A, Day 36 for Part B, and through Day 11 for Part D. Time will be represented proportionally on the x-axis.

Hematology, clinical chemistry, urinalysis, and coagulation (Part B and D) laboratory results will be presented in data listings for subjects in the safety analysis set. The listing will include the classification of low, normal, or high, the reference range, and the clinical significance. Classification of low, normal, and high laboratory values in the data listings will be based on the global laboratory reference ranges used across all sites. Clinical significance will be assessed for out of range values based on local laboratory reference ranges. Reference ranges provided in the data listings will be the global laboratory reference ranges used across all sites.

Pregnancy results will also be presented in a data listing for subjects in the safety analysis set.

9.6 Vital Signs, Physical Findings, and Other Observations Related to Safety

9.6.1 Vital Signs

Baseline and all post-baseline visit values and change from baseline to post-baseline values in systolic blood pressure, diastolic blood pressure, pulse rate, respiratory rate, temperature, weight, and pulse oximetry will be summarized for the safety analysis set for each study part by dose group using descriptive statistics, as described in Section 3. Height and body mass index (BMI) at baseline will be summarized for the safety analysis set for each study part by dose group using descriptive statistics, as described in Section 3.

Temperature results for each subject at each visit, through Day 7 for Part A subjects, through Day 36 for Part B subjects, and through Day 11 for Part D subjects, by study part and dose group will be provided in a line plot.

Vital sign results will be presented in a data listing for subjects in the safety analysis set.

9.6.2 Physical Examinations

The number and percentage of subjects at each visit with normal, abnormal not clinically significant and abnormal clinically significant physical exam findings for each body system will be summarized for each study part by dose group for the safety analysis set.

Physical examination results will be presented in a data listing for subjects in the safety analysis set.

9.6.3 Other Safety Measures

9.6.3.1 Electrocardiogram Findings

Shifts from baseline to post-baseline visits for each study part by dose group will be presented for normal, abnormal not clinically significant and abnormal clinically significant ECG findings, as determined by investigator interpretation, for the safety analysis set. Baseline for ECG findings is defined in Section 3.

Electrocardiogram findings will be presented in a data listing for subjects in the safety analysis set.

9.6.3.2 Spirometry

Baseline and all post-baseline visit values and change (absolute and relative) from baseline to post-baseline values for FEV_1, percent predicted FEV_1, FVC, percent predicted FVC, FEV_1/FVC, $FEF_{25-75\%}$, and PEF will be summarized for the safety analysis set using

descriptive statistics, as described in Section 3. . Baseline for all spirometry parameters is defined in Section 3.

Percent predicted FEV_1 results for each subject at each visit by study part and dose group will be provided in line plots for all visits and separately for visits up to Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively. These plots will be provided by dose group (4 mg [Part D only], 8 mg, 12 mg [Part B only], 16 mg, 20 mg, 24 mg [Part A only], and pooled placebo). Additionally, the mean values with standard error for each of the 4 mg dose group (Part D only), 8 mg dose group, 12 mg dose group (Part B only), 16 mg dose group, 20 mg dose group, 24 mg dose group (Part A only), and pooled placebo group will be provided in a line plot for percent predicted FEV_1 results for all visits and separately for visits up to Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively. The mean change (absolute and relative) from baseline values with standard error for each of the 4 mg dose group (Part D only), 8 mg dose group, 12 mg dose group (Part B only), 16 mg dose group, 20 mg dose group, 24 mg dose group (Part A only), and pooled placebo group will be provided in a line plot for percent predicted FEV_1 results for all post-baseline visits. These line plots will be provided separately for visits up to Day 29, Day 57, and Day 32 for Part A, Part B, and Part D, respectively. Time will be represented proportionally on the x-axis for the Part A and D FEV_1 figures.

Spirometry results will be presented in a data listing for subjects in the safety analysis set.

9.6.3.3 Chest X-ray

Shifts from baseline to post-baseline visits for each study part by dose group will be presented for normal, abnormal not clinically significant and abnormal clinically significant assessments for the safety analysis set. Chest x-ray findings will be presented in a data listing for subjects in the safety analysis set.

9.6.3.4 Prior and Concomitant Medications and Procedures

The prior and concomitant medications will be coded using the latest version of World Health Organization Drug Dictionary (WHO Drug) Global (2020-SEP) to identify the drug class and preferred drug name.

Concomitant medications will include all medications that started on or after day of first dose of the study drug or that stopped on or after day of first dose of study drug, including medications that are classified as ongoing. Prior medications will include all medications that started and stopped prior to the day of first dose of the study drug. Any medication with a missing stop date (i.e., day, month, and year are missing) will be classified as ongoing. For a medication with a missing start date, the medication will be classified as both a prior and concomitant medication unless the stop date is prior the date of first dose of study drug, in which case the medication will be classified as a prior medication. For medications with start date prior to the date of first dose of study drug and missing end date, the medication will be classified as both prior and concomitant. Medications with missing start and stop dates will be classified as prior and concomitant.

The number and percentage of subjects using prior medications, and separately concomitant medications, will be tabulated by Anatomical Therapeutic Chemical (ATC) level 1 term, ATC level 2 term, and preferred drug name for all subjects in the safety analysis set by study part and dose group, and also for the study overall. If a subject has more than 1 medication within an ATC level 1 term, the subject will be counted only once in that ATC level 1 term. Similarly, if a subject has more than 1 medication within an ATC level 2 term, the subject will be counted only once in that ATC level 2 term. If a subject has more than 1 medication that codes to the same preferred drug name, the subject will be counted only once for that preferred drug name. All percentages will use the number of subjects in the safety analysis set as the denominator. The tabular summaries will be sorted by overall (MRT5005 + Placebo) descending frequency by ATC level 1 term, ATC level 2 term, and preferred drug name.

Prior and concomitant medication data will also be presented in a data listing for subjects in the safety analysis set.

Concomitant surgical procedures will also be presented in a data listing for subjects in the safety analysis set.

9.6.3.5 Serum Inflammatory Markers

Serum samples will be analyzed for various inflammatory markers for only Part B 20 mg and Part D subjects.

Baseline and all post-baseline visit values and change from baseline to post-baseline for the inflammatory marker parameters will be summarized for the safety analysis set for each study part by dose group using descriptive statistics, as described in Section 3.

Serum inflammatory marker results will be presented in a data listing for Part B 20 mg and Part D subjects in the safety analysis set.

10. PHARMACOKINETIC EVALUATION

Analyses of pharmacokinetic samples (CFTR mRNA and [redacted]) are outside the scope of the SAP.

11. OTHER ANALYSES

11.1 Cystic Fibrosis Questionnaire-Revised (CFQ-R)

For Part B, the CFQ-R respiratory domain scores at baseline (Day -1) and Days 36, 43, 57, 85, 113, 197, 281, and 365 will be summarized for the safety analysis set by dose group using descriptive statistics, as described in Section 3. Change from baseline to post-baseline in CFQ-R respiratory domain scores will be calculated for each subject with data at baseline and the post-baseline visit. The mean change from baseline will be summarized for the safety analysis set by dose group at Days 36, 43, 57, 85, 113, 281, and 365.

CFQ-R respiratory domain scores at each visit will be presented in a data listing for Part B subjects in the safety analysis set.

12. CHANGES TO THE ANALYSES PLANNED IN THE PROTOCOL

Not applicable.

13. REFERENCES

US Federal Register. (1998) International Conference on Harmonization; Guidance for Industry: Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration. Federal Register, Vol. 63, No. 179, September 16, 1998, page 49583.

US Federal Register. (1996) International Conference on Harmonization; Guidance for Industry: Structure and Content of Clinical Study Reports. Department of Health and Human Services: Food and Drug Administration. Federal Register Vol. 61, July 17, 1996, page 37320.

14. LIST OF PLANNED TABLES

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
DM_TAA_F_X	14.1.1.1	Summary of Demographic and Baseline Characteristics by Dose Group	Safety Analysis Set	A, B, D, O
DS_TAA_F_X	14.1.3.1	Summary of Screen Failures	Screened Subjects	A, B, D, O
DS_TAB_F_X	14.1.3.2	Summary of Subject Disposition by Dose Group	Safety Analysis Set	A, B, D, O
EX_TAA_F_X	14.1.4	Summary of Investigational Product Administration by Dose Group	Safety Analysis Set	A, B, D, O
MH_TAA_F_X	14.1.5	Medical History by System Organ Class and Preferred Term by Dose Group	Safety Analysis Set	A, B, D, O
PD_TAA_F_X	14.1.6	Protocol Deviations by Type and Dose Group	Safety Analysis Set	A, B, D
AE_TAA_F_X	14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events by Dose Group	Safety Analysis Set	A, B, D
AE_TAI_F_A	14.3.1.1.1	Overall Summary of Treatment-Emergent Adverse Events by Dose Group Through Day 29	Safety Analysis Set	A
AE_TAI_F_B	14.3.1.1.1	Overall Summary of Treatment-Emergent Adverse	Safety Analysis Set	B

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
		Events by Dose Group Through Day 57		
AE_TAI_F_D	14.3.1.1.1	Overall Summary of Treatment-Emergent Adverse Events by Dose Group Through Day 32	Safety Analysis Set	D
AE_TAK_F_O	14.3.1.1.2	Overall Summary of Treatment-Emergent Adverse Events by Time Interval	Safety Analysis Set	O
AE_TAB_F_X	14.3.1.2	Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Time Interval and Dose Group	Safety Analysis Set	A, B, D
AE_TAC_F_X	14.3.2.1	Summary of Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term by Time Interval and Dose Group	Safety Analysis Set	A, B, D
AE_TAL_F_X	14.3.2.2	Summary of Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term by Time Interval and Dose Group	Safety Analysis Set	A, B, D
AE_TAE_F_X	14.3.2.3	Summary of Treatment-	Safety Analysis Set	A, B, D

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
		Emergent Adverse Events Classified as Pulmonary Exacerbations by System Organ Class and Preferred Term by Time Interval and Dose Group		
AE_TAH_F_X	14.3.1.3	Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group	Safety Analysis Set	A, B, D
AE_TAJ_F_A	14.3.1.3.1	Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 29	Safety Analysis Set	A
AE_TAJ_F_B	14.3.1.3.1	Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 57	Safety Analysis Set	B
AE_TAJ_F_D	14.3.1.3.1	Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 32	Safety Analysis Set	D
AE_TAN_F_O	14.3.1.4	Number of Treatment-Emergent Adverse Events by Preferred Term and Time Interval	Safety Analysis Set	O

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
AE_TAM_F_X	14.3.2.4	Summary of Treatment-Emergent Febrile Reactions in First 24 Hours After Completion of Nebulization by Preferred Term and Dose Group	Safety Analysis Set	A, B, D
AE_TAO_F_O	14.3.2.5	Summary of Treatment-Emergent Febrile Reactions in First 24 Hours After Completion of Nebulization by Preferred Term	Safety Analysis Set	O
AE_TAP_F_X	14.3.2.6	Summary of Treatment-Emergent Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Preferred Term and Dose Group	Safety Analysis Set	A, B, D
AE_TAQ_F_O	14.3.2.7	Summary of Treatment-Emergent Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Preferred Term	Safety Analysis Set	O
LB_TAA_F_X	14.3.4.1	Mean and Mean Change from Baseline in Chemistry Laboratory Values	Safety Analysis Set	A, B, D

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
		by Visit and Dose Group		
LB_TAB_F_X	14.3.4.2	Mean and Mean Change from Baseline in Hematology Laboratory Values by Visit and Dose Group	Safety Analysis Set	A, B, D
LB_TAE_F_B LB_TAE_F_D	14.3.4.3	Mean and Mean Change from Baseline in Serum Inflammatory Markers by Visit and Dose Group	Safety Analysis Set	B, D
VS_TAA_F_X	14.3.5.1	Mean and Mean Change from Baseline in Vital Signs by Visit and Dose Group	Safety Analysis Set	A, B, D
EG_TAA_F_ X	14.3.6.1	Shift in Electrocardiogram Findings by Visit and Dose Group	Safety Analysis Set	A, B, D
CX_TAA_F_X	14.3.7.1	Shift in Chest X-Ray by Visit and Dose Group	Safety Analysis Set	A, B, D
PE_TAA_F_X	14.3.8.1	Summary of Physical Examination by Visit and Dose Group	Safety Analysis Set	A, B, D
RE_TAA_F_X	14.3.9.1	Mean and Mean Absolute Change from Baseline in Spirometry Values by Visit and Dose Group	Safety Analysis Set	A, B, D
RE_TAB_F_X	14.3.9.2	Mean and Mean Relative Change from Baseline in	Safety Analysis Set	A, B, D

Rho Table Identifier[a]	Table No.[b]	Title	Population	Part
		Spirometry Values by Visit and Dose Group		
CM_TAA_F_X	14.3.10.1	Number and Percentage of Subjects with Concomitant Medications by Anatomic Class, Therapeutic Class, Medication Term, and Dose Group	Safety Analysis Set	A, B, D, O
CM_TAB_F_X	14.3.10.2	Number and Percentage of Subjects with Prior Medications by Anatomic Class, Therapeutic Class, Medication Term and Dose Group	Safety Analysis Set	A, B, D, O
QS_TAA_F_B	14.4.1	Mean and Mean Change from Baseline in CFQ-R Respiratory Domain Scores by Visit and Dose Group	Safety Analysis Set	B

[a]The same set of tables will be produced separately for each study part, unless otherwise specified. '_X' in each table name will reflect each study part (_A, _B, _D) or overall (_O). These tables will have the 'Dose Group' portion of the title removed.

[b] A, B, D or O will be added to each display number.

15. LIST OF PLANNED FIGURES

Rho Figure Identifier[a]	Figure No.[b]	Title	Population	Part
LB_FAA_F_X	14.3.4.1.1	C Reactive Protein (mg/L) by Dose Group, Subject, and Visit	Safety Analysis Set	A, B, D
LB_FAJ_F_A	14.3.4.1.1.1	C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 29	Safety Analysis Set	A
LB_FAJ_F_B	14.3.4.1.1.1	C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 57	Safety Analysis Set	B
LB_FAJ_F_D	14.3.4.1.1.1	C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 32	Safety Analysis Set	D
LB_FAB_F_X	14.3.4.2.1	White Blood Cells (x10^9/L) by Dose Group, Subject, and Visit	Safety Analysis Set	A, B, D
LB_FAC_F_X	14.3.4.3.1	Neutrophils/Leukocytes (%) by Dose Group, Subject, and Visit	Safety Analysis Set	A, B, D
VS_FAA_F_A	14.3.5.1.1	Body Temperature Values by Dose Group, Subject, and Visit Through Day 7	Safety Analysis Set	A
VS_FAA_F_B	14.3.5.1.1	Body Temperature Values by Dose Group, Subject, and Visit Through Day 36	Safety Analysis Set	B
VS_FAA_F_D	14.3.5.1.1	Body Temperature Values by Dose Group, Subject, and Visit Through Day 11	Safety Analysis Set	D
RE_FAH_F_X	14.3.9.1.2	Percent Predicted FEV1 Values by Dose Group, Subject, and Visit	Safety Analysis Set	A, B, D
RE_FAI_F_A	14.3.9.2.2	Percent Predicted FEV1 Values to Day 29 by Dose Group, Subject, and Visit	Safety Analysis Set	A
RE_FAI_F_B	14.3.9.2.2	Percent Predicted FEV1 Values to Day 57 by Dose Group, Subject, and Visit	Safety Analysis Set	B

Rho Figure Identifier[a]	Figure No.[b]	Title	Population	Part
RE_FAI_F_D	14.3.9.2.2	Percent Predicted FEV1 Values to Day 32 by Dose Group, Subject, and Visit	Safety Analysis Set	D
RE_FAC_F_X	14.3.9.3	Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit	Safety Analysis Set	A, B, D
RE_FAS_F_A	14.3.9.3.1	Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 29	Safety Analysis Set	A
RE_FAS_F_B	14.3.9.3.1	Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 57	Safety Analysis Set	B
RE_FAS_F_D	14.3.9.3.1	Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 32	Safety Analysis Set	D
RE_FAL_F_X	14.3.9.4	Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit	Safety Analysis Set	A, B, D
RE_FAM_F_A	14.3.9.4.1	Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 29	Safety Analysis Set	A
RE_FAM_F_B	14.3.9.4.1	Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 57	Safety Analysis Set	B
RE_FAM_F_D	14.3.9.4.1	Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 32	Safety Analysis Set	D

Rho Figure Identifier[a]	Figure No.[b]	Title	Population	Part
RE_FAN_F_X	14.3.9.4.2	Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit	Safety Analysis Set	A, B, D
RE_FAP_F_A	14.3.9.4.3	Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 29	Safety Analysis Set	A
RE_FAP_F_B	14.3.9.4.3	Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 57	Safety Analysis Set	B
RE_FAP_F_D	14.3.9.4.3	Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 32	Safety Analysis Set	D

[a]The same set of figures will be separately for each study part, unless otherwise specified. '_X' in each table name will reflect each study part (_A, _B, _D).
[b] A, B or D will be added to each display number.

16. LIST OF PLANNED DATA LISTINGS

Rho Listing Identifier[a]	Listing No.[b]	Title	Population	Part
DS_LAA_F_X	16.2.1.1	Listing of Screen Failures	Screened Subjects	A, B, D
DS_LAB_F_X	16.2.1.2	Listing of Subject Disposition	Safety Analysis Set	A, B, D
DS_LAC_F_X	16.2.1.3	Listing of Visits Not Done, Conducted as Home Health Visits, or Visits Conducted as Telephone Visits as a Replacement for a Scheduled In-Clinic Visit	Safety Analysis Set	A, B, D
PD_LAA_F_X	16.2.2	Listing of Protocol Deviations	Safety Analysis Set	A, B, D
DM_LAB_F_X	16.2.4.1	Listing of Demographics and Baseline Characteristics	Safety Analysis Set	A, B, D
EX_LAB_F_B EX_LAB_F_D	16.2.5.1	Listing of Overall Extent of Exposure	Safety Analysis Set	B, D
EX_LAC_F_X	16.2.5.2	Listing of Extent of Exposure at the Visit Level	Safety Analysis Set	A, B, D
EX_LAA_F_X	16.2.5.3	Listing of Investigational Product Administration	Safety Analysis Set	A, B, D
MH_LAA_F_X	16.2.6.1	Listing of Medical History by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAA_F_X	16.2.7.1	Listing of Adverse Events by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAB_F_X	16.2.7.2	Listing of Adverse Events Leading to Treatment Discontinuation by Subject, System Organ	Safety Analysis Set	A, B, D

Rho Listing Identifier[a]	Listing No.[b]	Title	Population	Part
		Class, and Preferred Term		
AE_LAD_F_X	16.2.7.3	Listing of Adverse Events Resulting in Death by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAC_F_X	16.2.7.4	Listing of Serious Adverse Events by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAL_F_X	16.2.7.5	Listing of Adverse Events of Special Interest by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAF_F_X	16.2.7.6	Listing of Adverse Events Classified as Pulmonary Exacerbations (Investigator and Protocol-Defined) by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAI_F_X	16.2.7.7	Listing of Pyrexia or Elevated Body Temperature Adverse Events Reported During and Up To 24 Hours After Completion of Nebulization by Subject, System Organ Class, and Preferred Term	Safety Analysis Set	A, B, D
AE_LAJ_F_X	16.2.7.8	Listing of Adverse Events Reported During and Up To 24 Hours After Completion of	Safety Analysis Set	A, B, D

Rho Listing Identifier[a]	Listing No.[b]	Title	Population	Part
		Nebulization by Subject, System Organ Class, and Preferred Term		
AE_LAK_F_X	16.2.7.9	Listing of Febrile Reactions and Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Subject and Preferred Term	Safety Analysis Set	A, B, D
LB_LAA_F_X	16.2.8.1	Listing of Chemistry Values	Safety Analysis Set	A, B, D
LB_LAB_F_X	16.2.8.2	Listing of Hematology Values	Safety Analysis Set	A, B, D
LB_LAC_F_X	16.2.8.3	Listing of Urinalysis Values	Safety Analysis Set	A, B, D
LB_LAD_F_B, LB_LAD_F_D	16.2.8.4	Listing of Coagulation Values	Safety Analysis Set	B, D
LB_LAE_F_B LB_LAE_F_D	16.2.8.5	Listing of Serum Inflammatory Markers	Safety Analysis Set	B, D
PG_LAA_F_X	16.2.8.8	Listing of Pregnancy Results	Safety Analysis Set	A, B, D
VS_LAA_F_X	16.2.9.1	Listing of Vital Signs	Safety Analysis Set	A, B, D
EG_LAA_F_X	16.2.10.1	Listing of Overall Electrocardiogram Interpretation Findings	Safety Analysis Set	A, B, D
CX_LAA_F_X	16.2.11.1	Listing of Chest X-Ray Findings	Safety Analysis Set	A, B, D
PE_LAA_F_X	16.2.12.1	Listing of Physical Examination Results	Safety Analysis Set	A, B, D
RE_LAA_F_X	16.2.13.1	Listing of Spirometry Values	Safety Analysis Set	A, B, D
CM_LAA_F_X	16.2.14.1	Listing of Prior and Concomitant Medications	Safety Analysis Set	A, B, D

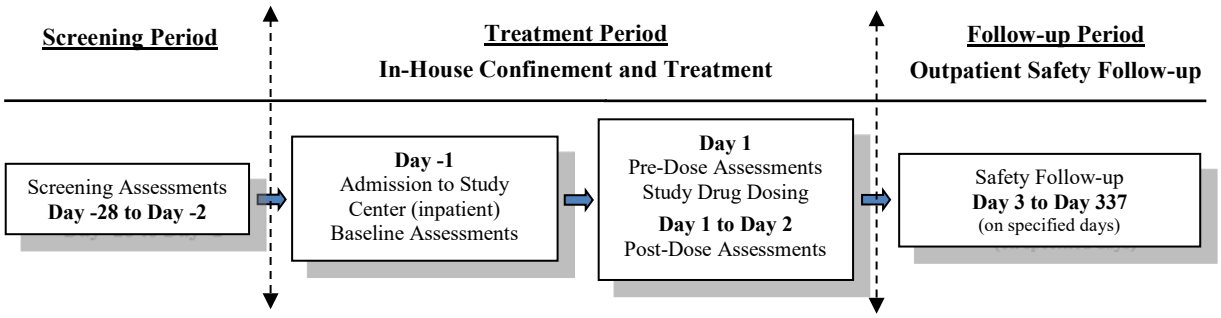
Rho Listing Identifier[a]	Listing No.[b]	Title	Population	Part
CM_LAB_F_X	16.2.14.2	Listing of Concomitant Surgical Procedures	Safety Analysis Set	A, B, D
QS_LAA_F_B	16.2.15.1	Listing of CFQ-R Respiratory Domain Scores	Safety Analysis Set	B

[a]The same set of listings will be separately for each study part, unless otherwise specified. '_X' in each table name will reflect each study part (_A, _B, _D).
[b]A, B or D will be added to each display number.

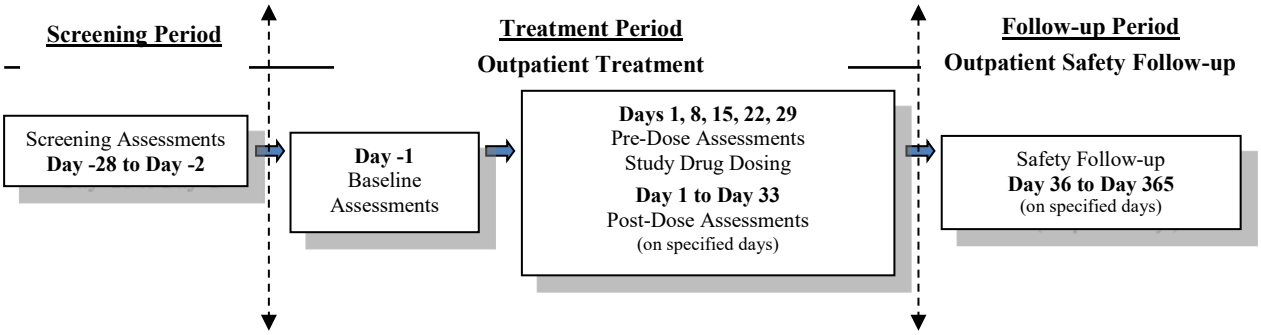
17. APPENDICES

17.1 Study Flow Chart

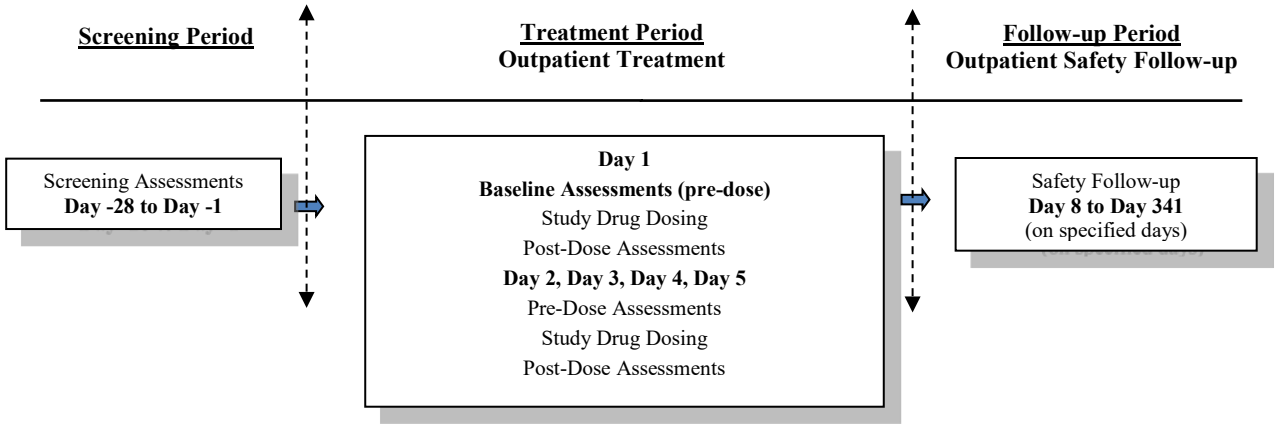
Part A



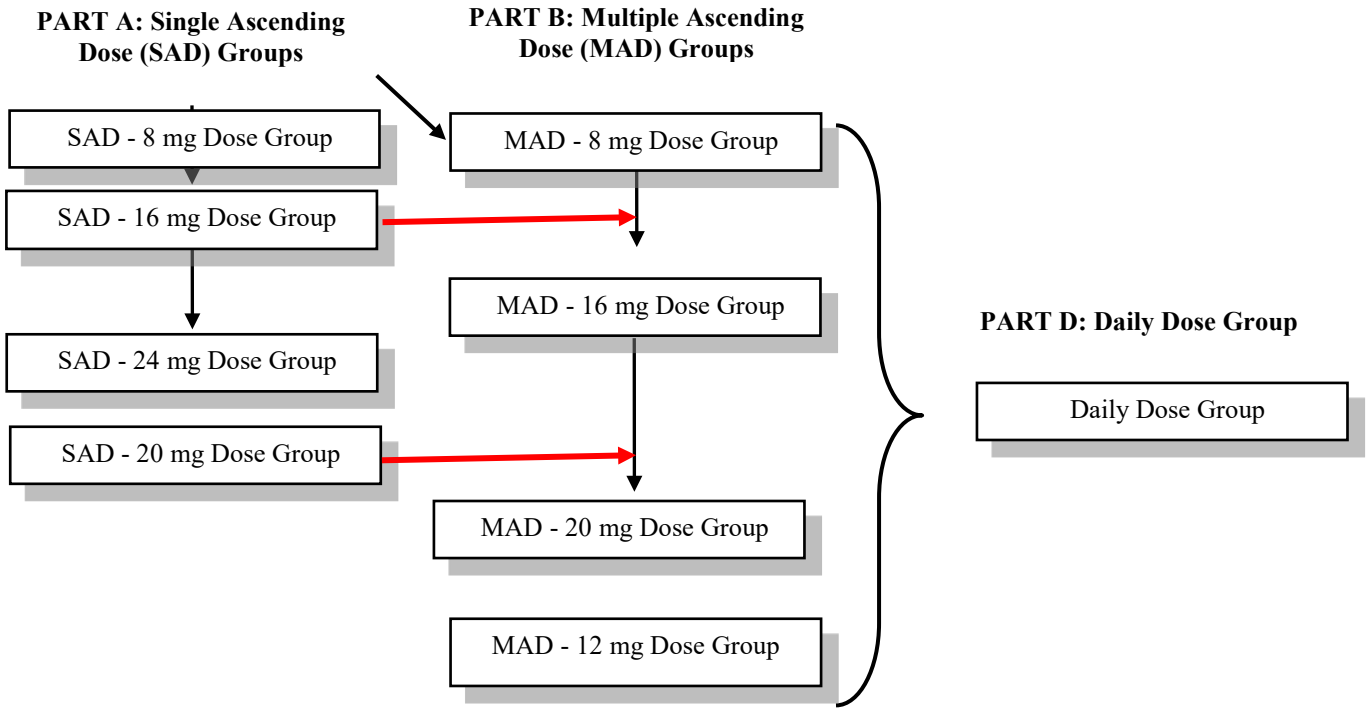
Part B



Part D



17.2 Subject Enrollment and Treatment Allocation



17.3 Schedule of Events

The schedule of events is outlined in Table 1 through Table 9 in the protocol.

18. ATTACHMENTS

- Table Display Specifications
- Listing Display Specifications
- Figure Display Specifications

Translate Bio, Inc.
PROTOCOL NUMBER MRT5005-101

A Phase 1/2, Randomized, Double-Blind, Placebo-Controlled, Combined Single and Multiple Ascending Dose Study Evaluating the Safety, Tolerability, and Biological Activity of MRT5005 ([redacted] mRNA/[redacted] LNP) Administered by Nebulization to Adult [redacted] with [redacted] ic Fibrosis

Table Specifications

VERSION DATE: 26 October 2021

SPONSOR: Translate Bio, Inc.
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Table Specifications

Table of Contents

General Programming Notes

The following instructions apply to all table displays.

DISPLAY OUTPUTS FOR EACH PART
Each table will be produced for each study part (A, B, D), unless otherwise specified. Each version of the table will include the relevant study part in the header and in the table identifier. For example, DM_TAA_F_X will be identified as DM_TAA_F_A for Part A and will include a header to show 'Part A'. Certain tables will also be produced for the study overall (O). For the overall tables, 'Part: All Study Parts' will print in the header and _O will be appended to the table identifier. A, B, D or O will be added to each display number.

PROGRAMMER NOTES

Programmer notes appear at the bottom of each table display shell where applicable.

Dose groups for each part are as follow:

- Part A: MRT5005 8mg, MRT5005 16mg, MRT5005 20mg, MRT5005 24mg, Pooled Placebo
- Part B: MRT5005 8mg, MRT5005 12mg, MRT5005 16mg, MRT5005 20mg, Pooled Placebo
- Part D: MRT5005 4mg, Placebo

For the overall tables, the treatment groups will be Pooled MRT5005 and Pooled Placebo.

Column labels in the mock tables use MRT5005 Xmg and Pooled Placebo. For Part D tables, Placebo should be used and not Pooled Placebo.

PAGE FORMATTING

The specifications for the format of each page are page size=47, line size=134, font=Courier, font size=8, and margin = 1.5" top, 1" bottom, left, and right.

"Listing Source: <Listing Number>" will be printed on the right side of the footer for each table.

PRECISION

No preliminary rounding should be performed; rounding should only occur after analysis. To round, consider digit to right of last significant digit: if < 5 then round down, if ≥ 5 then round up. Means, medians, 25th percentiles, 75th percentiles, and confidence intervals will be presented with one more decimal place than the precision of the data. Standard deviations will be presented with two more decimal places than the precision of the data. Percentages will be presented with one

decimal place. Minimums and maximums will be presented with the same precision as the original data, with a maximum of 4 decimal places.

Demographics

Table 14.1.1.1 (DM_TAA_F_X)
Summary of Demographic and Baseline Characteristics by Dose Group
Population: Safety Analysis Set

Part: x Characteristics	MRT5005 Xmg N=xx	MRT5005 Xmg N=xx	MRT5005 Xmg N=xx	Pooled Placebo N=xx
Sex – n (%)				
Male	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Age (years) [1]				
Subject 1	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx
Race – n (%)				
White	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
American Indian or Alaska Native	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Reported	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity – n (%)				
Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Not Reported	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Genotype – n (%)				
Class I/Class I	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Class I/Class II	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Class II/Class I	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Class II/Class II	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Missing/xxxx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
CFTR Modulator Use at Baseline – n (%) [2]				
Yes	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Percent Predicted FEV_1 at Baseline – n (%) [3]				
< 70	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
≥ 70	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] DM_F01
[2] DM_F02
[3] RE_F01
AB_F02
PC_F02

Listing Source: DM_LAB_F_X

Notes:

1) ***'Missing' row should only be included for categorical variables if there is missing data. For genotype, if only one class is missing, still display the populated mutation (i.e. Missing/Class I).***
2) ***The Missing row should be included in the %s.***
3) ***For Part D, replace footnote RE_F01 with RE_F01D.***

Table 14.1.1.1 (DM_TAA_F_O)
Summary of Demographic and Baseline Characteristics
Population: Safety Analysis Set

Part: All Study Parts Characteristics	Pooled MRT5005 N=xx	Pooled Placebo N=xx
Sex – n (%)		
Male	xx (xx.x)	xx (xx.x)
Female	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Age (years) [1]		
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Range	(xx, xx)	(xx, xx)
Race – n (%)		
White	xx (xx.x)	xx (xx.x)
Black or African American	xx (xx.x)	xx (xx.x)
Asian	xx (xx.x)	xx (xx.x)
American Indian or Alaska Native	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	xx (xx.x)	xx (xx.x)
Not Reported	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Ethnicity – n (%)		
Hispanic or Latino	xx (xx.x)	xx (xx.x)
Not Hispanic or Latino	xx (xx.x)	xx (xx.x)
Not Reported	xx (xx.x)	xx (xx.x)
Missing	xx (xx.x)	xx (xx.x)
Genotype – n (%)		
Class I/Class I	xx (xx.x)	xx (xx.x)
Class I/Class II	xx (xx.x)	xx (xx.x)
Class II/Class I	xx (xx.x)	xx (xx.x)
Class II/Class II	xx (xx.x)	xx (xx.x)
Missing/xxxx	xx (xx.x)	xx (xx.x)

Etc.	xx (xx.x)	xx (xx.x)
CFTR Modulator Use at Baseline – n (%) [2]		
Yes	xx (xx.x)	xx (xx.x)
No	xx (xx.x)	xx (xx.x)
Percent Predicted FEV_1 at Baseline – n (%) [3]		
< 70	xx (xx.x)	xx (xx.x)
≥ 70	xx (xx.x)	xx (xx.x)
Percent Predicted FEV_1 at Baseline [3]		
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Range	(xx, xx)	(xx, xx)

[1] DM_F01
[2] DM_F02
[3] RE_F01O
AB_F02
PC_F02

Listing Source: DM_LAB_F_X

Notes:

1) ***'Missing' row should only be included for categorical variables if there is missing data. For genotype, if only one class is missing, still display the populated mutation (i.e. Missing/Class I).***
2) ***The Missing row should be included in the %s.***

Disposition

Table 14.1.3.1 (DS_TAA_F_X)
Summary of Screen Failures
Population: Screened Subjects

	Total N=xx n (%)
Screened	xx
Screen failure	xx (xx.x)
Randomized	xx (xx.x)
Reason for screen failure	
Adverse Event	
Inclusion/exclusion	xx (xx.x)
Lost to follow-up	xx (xx.x)
Withdrew consent	xx (xx.x)
Other	xx (xx.x)

Note: PC_F02

Listing Source: DS_LAA_F_X

Notes:

1) ***Please check footnotes for denominators.***
2) ***DS_TAA_F_X will be produced for each study part and for the study overall.***

Table 14.1.3.2 (DS_TAB_F_X)
Summary of Subject Disposition by Dose Group
Population: Safety Analysis Set

Part: x	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Study completion status [1]				
Completed	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Discontinued	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for premature study discontinuation [2]				
Adverse event	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Investigator decision	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pregnancy	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study terminated by sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal of consent	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] PC_F02
[2] DS_F03

Listing Source: DS_LAB_F_X

Notes:
1) Please check footnotes for denominators.
2) DS_TAB_F_X will be produced for each study part and for the study overall.

Treatment Compliance

Table 14.1.4 (EX_TAA_F_X)
Summary of Investigational Product Administration by Dose Group
Population: Safety Analysis Set

Part: x	MRT5005 Xmg N=xx	MRT5005 Xmg N=xx	MRT5005 Xmg N=xx	Pooled Placebo N=xx
Number of Total Doses Administered – n (%)				
1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
5	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Full Doses Administered				
Subject 1	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx
Number of Partial Doses Administered				
Subject 1	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx

AB_F01a
PC_F02
EX_F01

Listing Source: EX_LAB_F_X, EX_LAC_F_X

Notes:

1) ***For Part A, only display the category for 1 Total Dose Administered, and do not present the summary statistics. For Parts B and D, please display all categories for number of doses administered (1-5) and summary statistics. The number of doses section is the sum of full and partial doses.***

Table 14.1.4 (EX_TAA_F_O)
Summary of Investigational Product Administration
Population: Safety Analysis Set

Part: All Study Parts	Pooled MRT5005 N=xx	Pooled Placebo N=xx
Number of Total Doses Administered - n (%)		
1	xx (xx.x)	xx (xx.x)
2	xx (xx.x)	xx (xx.x)
3	xx (xx.x)	xx (xx.x)
4	xx (xx.x)	xx (xx.x)
5	xx (xx.x)	xx (xx.x)
Number of Full Doses Administered		
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Range	(xx, xx)	(xx, xx)
Number of Partial Doses Administered		
Mean	xx.x	xx.x
SD	xx.xx	xx.xx
Range	(xx, xx)	(xx, xx)

AB_F01
PC_F02
EX_F01

Listing Source: EX_LAB_F_X, EX_LAC_F_X

Medical History

Table 14.1.5 (MH_TAA_F_X)
Medical History by System Organ Class and Preferred Term by Dose Group
Population: Safety Analysis Set

Part: x

System Organ Class Preferred Term	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Any Medical History	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PC_F02
MH_F01

Listing Source: MH_LAA_F_X

Notes:

1) ***MH_TAA_F_X will be produced for each study part and for the study overall.***
2) ***Sort System Organ Class and Preferred Term within System Organ Class by descending order of overall (MRT5005 + Placebo) frequency.***

Protocol Deviations

Table 14.1.6 (PD_TAA_F_X)
Protocol Deviations by Type and Dose Group
Population: Safety Analysis Set

Part: x Type	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Any Protocol Deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Type 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Type 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Type 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

PC_F02

Listing Source: PD_LAA_F_X

Notes:
1) PD_TAA_F_X will be produced for each study part.
2) Sort Type by descending order of overall (MRT5005 + Placebo) frequency.

Adverse Events

Table 14.3.1.1 (AE_TAA_F_X)
Overall Summary of Treatment-Emergent Adverse Events by Dose Group
Population: Safety Analysis Set

Part: x	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Number of TEAEs Reported	xx	xx	xx	xx
Number of Subjects with Any TEAE Reported [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Serious TEAEs Reported	xx	xx	xx	xx
Number of Subjects with Any Serious TEAE Reported [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of TEAEs by Relationship to IP				
Not Related	xx	xx	xx	xx
Related	xx	xx	xx	xx
Number of Subjects with TEAEs by Relationship to IP [2]				
Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs by Relationship to Nebulization/Treatment Administration [3]				
Not Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Related	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of TEAEs by Severity				
Mild	xx	xx	xx	xx
Moderate	xx	xx	xx	xx
Severe	xx	xx	xx	xx
Number of Subjects with TEAEs by Severity [4]				
Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs Leading to Treatment Discontinuation [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs Resulting in Death [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of TEAEs Classified as a Pulmonary Exacerbation by Type				
All	xx	xx	xx	xx

Investigator-Defined	xx	xx	xx	xx
Protocol-Defined	xx	xx	xx	xx
Number of Subjects with TEAEs Classified as a Pulmonary Exacerbation by Type [1]				
All [5]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Investigator-Defined	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol-Defined	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

AB_F03
[1] AE_F05
[2] AE_F06a
[3] AE_F06b
[4] AE_F07
[5] AE_F06d
PC_F02

Listing Source: AE_LAA_F_X

Notes:

1) ***The rows 'Number of TEAEs Reported' and 'Number of Serious TEAEs Reported' display the total number of TEAE counts.***
2) ***If a subject experiences multiple adverse events, then take the closest relationship to study drug for the row 'Number of Subjects with TEAEs by Relationship' for each relationship to IP and relationship to nebulization***
3) ***If a subject experiences multiple adverse events, then take the worst case severity for the row 'Number of Subjects with TEAEs by Severity'.***
4) ***In the by type summary of subjects with TEAEs classified as pulmonary exacerbations, any subject with either investigator-defined or protocol-defined will be counted once in the All row. Subjects with both an investigator-defined and a protocol-defined TEAE classified as a pulmonary exacerbation will be recorded once in each row, investigator-defined and protocol-defined.***

Non-unique tables for AE_TAA_F_X:

Table 14.3.1.1.1 (AE_TAI_F_A)
Overall Summary of Treatment-Emergent Adverse Events by Dose Group Through Day 29
Population: Safety Analysis Set

AB_F03
[1] AE_F05
[2] AE_F06a
[3] AE_F06b
[4] AE_F07
[5] AE_F06d
PC_F02

Listing Source: AE_LAA_F_A

Table 14.3.1.1.1 (AE_TAI_F_B)
Overall Summary of Treatment-Emergent Adverse Events by Dose Group Through Day 57
Population: Safety Analysis Set

AB_F03
[1] AE_F05
[2] AE_F06a
[3] AE_F06b
[4] AE_F07
[5] AE_F06d
PC_F02

Listing Source: AE_LAA_F_B

Table 14.3.1.1.1 (AE_TAI_F_D)
Overall Summary of Treatment-Emergent Adverse Events by Dose Group Through Day 32
Population: Safety Analysis Set

AB_F03
[1] AE_F05
[2] AE_F06a
[3] AE_F06b
[4] AE_F07
[5] AE_F06d
PC_F02

Listing Source: AE_LAA_F_D

Table 14.3.1.1.2 (AE_TAK_F_O)
Overall Summary of Treatment-Emergent Adverse Events by Time Interval
Population: Safety Analysis Set

Part: x
Time Interval: xx to xx

	Pooled MRT5005 N=xx n (%)	Pooled Placebo N=xx n (%)
Number of TEAEs Reported	xx	xx
Number of Subjects with Any TEAE Reported [1]	xx (xx.x)	xx (xx.x)
Number of Serious TEAEs Reported	xx	xx
Number of Subjects with Any Serious TEAE Reported [1]	xx (xx.x)	xx (xx.x)
Number of TEAEs by Relationship to IP		
Not Related	xx	xx
Related	xx	xx
Number of Subjects with TEAEs by Relationship to IP [2]		
Not Related	xx (xx.x)	xx (xx.x)
Related	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs by Relationship to Nebulization/Treatment Administration [3]		
Not Related	xx (xx.x)	xx (xx.x)
Related	xx (xx.x)	xx (xx.x)
Number of TEAEs by Severity		
Mild	xx	xx
Moderate	xx	xx
Severe	xx	xx
Number of Subjects with TEAEs by Severity [4]		
Mild	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs Leading to Treatment Discontinuation [1]	xx (xx.x)	xx (xx.x)
Number of Subjects with TEAEs Resulting in Death [1]	xx (xx.x)	xx (xx.x)
Number of TEAEs Classified as a Pulmonary Exacerbation by Type		
All	xx	xx
Investigator-Defined	xx	xx

Protocol-Defined	xx	xx
Number of Subjects with TEAEs Classified as a Pulmonary Exacerbation by Type [1]		
All [5]	xx (xx.x)	xx (xx.x)
Investigator-Defined	xx (xx.x)	xx (xx.x)
Protocol-Defined	xx (xx.x)	xx (xx.x)

AB_F03
[1] AE_F05
[2] AE_F06a
[3] AE_F06b
[4] AE_F07
[5] AE_F06d
PC_F02
AE_F18

Listing Source: AE_LAA_F_X

Notes:

1) ***The first page will be "Part: All Study Parts" with "Time Interval: Overall" and will include all AEs across all study parts. The subsequent page will be: "Part: All Study Parts" with "Time Interval: 1 month post-dose". The last page will be: "Part: All Study Parts" with "Time Interval: > 1 month post-dose".***
2) ***In the column headers, report the number of subjects who were at risk for an AE at the start of the interval.***
3) ***The rows 'Number of TEAEs Reported' and 'Number of Serious TEAEs Reported' display the total number of TEAE counts.***
4) ***If a subject experiences multiple adverse events, then take the closest relationship to study drug for the row 'Number of Subjects with TEAEs by Relationship' for each relationship to IP and relationship to nebulization***
5) ***If a subject experiences multiple adverse events, then take the worst case severity for the row 'Number of Subjects with TEAEs by Severity'.***
6) ***In the by type summary of subjects with TEAEs classified as pulmonary exacerbations, any subject with either investigator-defined or protocol-defined will be counted once in the All row. Subjects with both an investigator-defined and a protocol-defined TEAE classified as a pulmonary exacerbation will be recorded once in each row, investigator-defined and protocol-defined.***

Table 14.3.1.2 (AE_TAB_F_X)
Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term by Time Interval and Dose Group
Population: Safety Analysis Set

Part: x
Time Interval: xx to xx

System Organ Class Preferred Term	MRT5005 Xmg N=xx n (%) m	MRT5005 Xmg N=xx n (%) m	MRT5005 Xmg N=xx n (%) m	Pooled Placebo N=xx n (%) m
System Organ Class 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Preferred Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Preferred Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
System Organ Class 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Preferred Term 1	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Preferred Term 2	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx

AB_F04
AE_F08
AE_F14
AE_F15
AE_F16

Listing Source: AE_LAA_F_X

Notes:

1) ***Repeat for each time interval. Time intervals for Part A are Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 29, Study Day > 29. Time intervals for Part B are Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 36, 1 ≤ Study Day ≤ 57, and Study Day > 57. Time intervals for Part D are Overall, Study Day 1, 1 < Study Day ≤ 5, 1 ≤ Study Day ≤ 11, 1 ≤ Study Day ≤ 32, and Study Day > 32.***
2) ***In the column headers, report the number of subjects who were at risk for an AE at the start of the interval.***
3) ***Sort System Organ Class and Preferred Term within System Organ Class by descending order of overall (MRT5005 + Placebo) frequency in subject counts.***
4) ***The number of events will be summarized such that subjects with multiple TEAEs in system organ class in a time interval are counted more than once. Subjects with multiple TEAEs in preferred term in a time interval are counted more than once.***

Non-unique tables for AE_TAB_F_X:

Table 14.3.2.1 (AE_TAC_F_X)
Summary of Treatment-Emergent Serious Adverse Events by System Organ Class and Preferred Term by Time Interval and Dose Group
Population: Safety Analysis Set

AB_F04
AE_F08
AE_F14
AE_F15
AE_F16

Listing Source: AE_LAC_F_X

Notes:
1) AE_TAC_F_X will be provided for each study part.
2) Repeat AE_TAB_F_X for Serious Adverse Events.

Table 14.3.2.2 (AE_TAL_F_X)
Summary of Treatment-Emergent Adverse Events of Special Interest by System Organ Class and Preferred Term by Time Interval and Dose Group
Population: Safety Analysis Set

AB_F04
AE_F08
AE_F14
AE_F15
AE_F16

Listing Source: AE_LAL_F_X

Notes:
1) AE_TAL_F_X will be provided for each study part.
2) Repeat AE_TAB_F_X for AESIs.

Table 14.3.2.3 (AE_TAE_F_X)
Summary of Treatment-Emergent Adverse Events Classified as Pulmonary Exacerbations by Preferred Term by Time Interval and Dose Group
Population: Safety Analysis Set

Part: x
Time Interval: xx to xx

Preferred Term Type	MRT5005 Xmg N=xx n (%) m	MRT5005 Xmg N=xx n (%) m	MRT5005 Xmg N=xx n (%) m	Pooled Placebo N=xx n (%) m
Preferred Term 1				
All	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Investigator-Defined	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Protocol-Defined	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Preferred Term 2				
All	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Investigator-Defined	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx
Protocol-Defined	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx	xx (xx.x) xx

AB_F04
AE_F09
AE_F14a
AE_F15
AE_F16

Listing Source: AE_LAF_F_X

Notes:

1) ***Repeat for each time interval. Time intervals for Part A are Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 29, Study Day > 29. Time intervals for Part B are Overall, Study Day 1, 1 < Study Day ≤ 7, 1 ≤ Study Day ≤ 36, 1 ≤ Study Day ≤ 57, and Study Day > 57. Time intervals for Part D are Overall, Study Day 1, 1 < Study Day ≤ 5, 1 ≤ Study Day ≤ 11, 1 ≤ Study Day ≤ 32, and Study Day > 32.***
2) ***In the column headers, report the number of subjects who were at risk for an AE at the start of the interval.***
3) ***Report pulmonary exacerbations by type (all, investigator-defined and protocol-defined).***
4) ***Sort Preferred Term by descending order of overall (MRT5005 + Placebo) frequency in subject counts.***
5) ***The number of events will be summarized such that subjects with multiple TEAEs in a preferred term in a time interval in a type are counted more than once.***

Table 14.3.1.3 (AE_TAH_F_X)
Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group
Population: Safety Analysis Set

Part: x Preferred Term	MRT5005 Xmg N=xx Events	MRT5005 Xmg N=xx Events	MRT5005 Xmg N=xx Events	Pooled Placebo N=xx Events
Preferred Term 1	xx	xx	xx	xx
Preferred Term 2	xx	xx	xx	xx
Preferred Term 3	xx	xx	xx	xx
Etc.				

AB_F04
AE_F09
AE_F14a
AE_F19

Listing Source: AE_LAA_F_X

Notes:
1) Sort by descending order of overall (MRT5005 + Placebo) frequency.
2) Summarize number of events, so subjects with multiple TEAEs in preferred term in a time interval are counted more than once.

Table 14.3.1.3.1 (AE_TAJ_F_A)
Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 29
Population: Safety Analysis Set

Part: x Preferred Term	MRT5005 8mg N=xx Events	MRT5005 16mg N=xx Events	MRT5005 20mg N=xx Events	MRT5005 24mg N=xx Events	Pooled Placebo N=xx Events
Preferred Term 1	xx	xx	xx	xx	xx
Preferred Term 2	xx	xx	xx	xx	xx
Preferred Term 3	xx	xx	xx	xx	xx
Etc.					

AB_F04
AE_F09
AE_F14a
AE_F19

Listing Source: AE_LAA_F_A

Notes:

1) ***Sort by descending order of overall (MRT5005 + Placebo) frequency.***
2) ***Summarize number of events, so subjects with multiple TEAEs in preferred term in a time interval are counted more than once.***

Table 14.3.1.3.1 (AE_TAJ_F_B)
Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 57
Population: Safety Analysis Set

Part: x Preferred Term	MRT5005 8mg N=xx Events	MRT5005 12mg N=xx Events	MRT5005 16mg N=xx Events	MRT5005 20mg N=xx Events	Pooled Placebo N=xx Events
Preferred Term 1	xx	xx	xx	xx	xx
Preferred Term 2	xx	xx	xx	xx	xx
Preferred Term 3	xx	xx	xx	xx	xx
Etc.					

AB_F04
AE_F09
AE_F14a
AE_F19

Listing Source: AE_LAA_F_B

Notes:

1) ***Sort by descending order of overall (MRT5005 + Placebo) frequency.***
2) ***Summarize number of events, so subjects with multiple TEAEs in preferred term in a time interval are counted more than once.***

Table 14.3.1.3.1 (AE_TAJ_F_D)
Number of Treatment-Emergent Adverse Events by Preferred Term by Dose Group Through Day 32
Population: Safety Analysis Set

Part: x Preferred Term	MRT5005 4mg N=xx Events	Placebo N=xx Events
Preferred Term 1	xx	xx
Preferred Term 2	xx	xx
Preferred Term 3	xx	xx
Etc.		

AB_F04

AE_F09
AE_F14a
AE_F19

Listing Source: AE_LAA_F_D

Notes:

1) ***Sort by descending order of overall (MRT5005 + Placebo) frequency.***
2) ***Summarize number of events, so subjects with multiple TEAEs in preferred term in a time interval are counted more than once.***

Table 14.3.1.4 (AE_TAN_F_O)
Number of Treatment-Emergent Adverse Events by Preferred Term and Time Interval
Population: Safety Analysis Set

Part: x
Time Interval: x

Preferred Term	Pooled MRT5005 N=xx Events	Pooled Placebo N=xx Events
Preferred Term 1	xx	xx
Preferred Term 2	xx	xx
Preferred Term 3	xx	xx
Etc.		

AB_F04
AE_F09
AE_F14a
AE_F19
AE_F18

Notes:

1) ***The first page will be "Part: All Study Parts" with "Time Interval: Overall" and will include all AEs across all study parts. The subsequent page will be: "Part: All Study Parts" with "Time Interval: 1 month post-dose"***
2) ***In the column headers, report the number of subjects who were at risk for an AE at the start of the interval.***
3) ***Sort by descending order of overall (Pooled MRT5005 + Pooled Placebo) frequency.***
4) ***Summarize number of events, so subjects with multiple TEAEs in preferred term in a time interval are counted more than once.***

Table 14.3.2.4 (AE_TAM_F_X)
Summary of Treatment-Emergent Febrile Reactions in First 24 Hours After Completion of Nebulization by Preferred Term and Dose Group
Population: Safety Analysis Set

	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Number of Febrile Reactions Reported	xx	xx	xx	xx
Number of Subjects with Any Febrile Reactions Reported [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Febrile Reactions by Severity [2]				
Mild	xx	xx	xx	xx
Moderate	xx	xx	xx	xx
Severe	xx	xx	xx	xx
Number of Subjects with Febrile Reactions by Maximum Severity [3]				
Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] AE_F05
[2] AE_F17c
[3] AE_F07a
Note: AE_F17a

Listing Source: AE_LAK_F_X

Notes:
1) AE_TAM_F_X will be produced for each study part.

Table 14.3.2.6 (AE_TAP_F_X)
Summary of Treatment-Emergent Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Preferred Term and Dose Group
Population: Safety Analysis Set

	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Pooled Placebo N=xx n (%)
Number of Hypersensitivity Reactions Reported	xx	xx	xx	xx
Number of Subjects with Any Hypersensitivity Reactions Reported [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Number of Hypersensitivity Reactions by Severity				
Mild	xx	xx	xx	xx
Moderate	xx	xx	xx	xx
Severe	xx	xx	xx	xx
Number of Subjects with Hypersensitivity Reactions by Maximum Severity [2]				
Mild	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] AE_F05
[2] AE_F07b
Note: AE_F17b

Listing Source: AE_LAK_F_X

Notes:
1) AE_TAM_F_X will be produced for each study part.

Table 14.3.2.5 (AE_TAO_F_O)
Summary of Treatment-Emergent Febrile Reactions in First 24 Hours After Completion of Nebulization by Preferred Term
Population: Safety Analysis Set

	Pooled MRT5005 N=xx n (%)	Pooled Placebo N=xx n (%)
Number of Febrile Reactions Reported	xx	xx
Number of Subjects with Any Febrile Reactions Reported [1]	xx (xx.x)	xx (xx.x)
Number of Febrile Reactions by Severity [2]		
Mild	xx	xx
Moderate	xx	xx
Severe	xx	xx
Number of Subjects with Febrile Reactions by Maximum Severity [3]		
Mild	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)

[1] AE_F05
[2] AE_F17c
[3] AE_F07a
Note: AE_F17a

Listing Source: AE_LAK_F_X

Table 14.3.2.7 (AE_TAQ_F_O)
Summary of Treatment-Emergent Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Preferred Term
Population: Safety Analysis Set

	Pooled MRT5005 N=xx n (%)	Pooled Placebo N=xx n (%)
Number of Hypersensitivity Reactions Reported	xx	xx
Number of Subjects with Any Hypersensitivity Reactions Reported [1]	xx (xx.x)	xx (xx.x)
Number of Hypersensitivity Reactions by Severity		
Mild	xx	xx
Moderate	xx	xx
Severe	xx	xx
Number of Subjects with Hypersensitivity Reactions by Maximum Severity [2]		
Mild	xx (xx.x)	xx (xx.x)
Moderate	xx (xx.x)	xx (xx.x)
Severe	xx (xx.x)	xx (xx.x)

[1] AE_F05
[2] AE_F07b
Note: AE_F17b

Listing Source: AE_LAK_F_X

Vital Signs

Table 14.3.5.1 (VS_TAA_F_X)
Mean and Mean Change from Baseline in Vital Signs by Visit and Dose Group
Population: Safety Analysis Set

Part: x Parameter (unit) Visit Statistic	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	Pooled Placebo N=xx Actual	 Absolute Change from Baseline
Parameter 1 (unit)								
Baseline								
Subject 1	xx		xx		xx		xx	
Subject 2	xx		xx		xx		xx	
Subject 3	xx		xx		xx		xx	
Subject 4	xx		xx		xx		xx	
Mean	xx.x		xx.x		xx.x		xx.x	
SD	xx.xx		xx.xx		xx.xx		xx.xx	
DAY 1 (0HRPOST-DOSE)								
Subject 1	xx	xx	xx	xx	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Etc.								

AB_F01a
BL_F01
CH_F01
VS_F01 (for Parts A and B)

Listing Source: VS_LAA_F_X

Notes:

1) ***Parameters include: Systolic Blood Pressure, Diastolic Blood Pressure, Pulse Rate, Respiratory Rate, Temperature, Height, Weight, BMI, Pulse Oximetry.***
2) ***Include all post-baseline visits/timepoints where vital signs are collected for Systolic Blood Pressure, Diastolic Blood Pressure, Pulse Rate, Respiratory Rate, Temperature, Weight, Pulse Oximetry.***
3) ***For any parameter collected multiple times during the nebulization period, select the latest 'DOSING' record for that dosing day.***
4) ***Include baseline only for Height and BMI.***
5) ***Exclude Part A Day 1 (Dosing) records.***

Laboratory Values

Non-unique tables for VS_TAA_F_X:

Table 14.3.4.1 (LB_TAA_F_X)
Mean and Mean Change from Baseline in Chemistry Laboratory Values by Visit and Dose Group
Population: Safety Analysis Set

AB_F01a
BL_F01
CH_F01

Listing Source: LB_LAA_F_X

Notes:

1) ***Parameters include: all chemistry laboratory test names, excluding beta-human chorionic gonadotropin***
2) ***Include all visits where chemistry laboratory tests are collected.***

Table 14.3.4.2 (LB_TAB_F_X)
Mean and Mean Change from Baseline in Hematology Laboratory Values by Visit and Dose Group
Population: Safety Analysis Set

AB_F01a
BL_F01
CH_F01

Listing Source: LB_LAB_F_X

Notes:

1) ***Parameters include: all hematology laboratory test names, excluding mean corpuscular hemoglobin and mean platelet volume.***
2) ***Include all visits where hematology laboratory tests are collected.***

Table 14.3.4.3 (LB_TAE_F_B, LB_TAE_F_D)
Mean and Mean Change from Baseline in Immune Response to Serum Inflammatory Markers by Visit and Dose Group
Population: Safety Analysis Set

AB_F01a
BL_F01
CH_F01

Listing Source: LB_LAG_F_B, LB_LAG_F_D

Notes:

1) ***Parameters include: all inflammatory marker***
2) ***Include all visits where inflammatory markers are collected.***

Electrocardiogram

Table 14.3.6.1 (EG_TAA_F_X)
Shift in Overall Electrocardiogram Interpretation Findings by Visit and Dose Group
Population: Safety Analysis Set

Part x	Baseline											
	MRT5005 Xmg N=xx			MRT5005 Xmg N=xx			MRT5005 Xmg N=xx			Pooled Placebo N=xx		
	Normal	Abnormal, NCS	Abnormal, CS	Normal	Abnormal, NCS	Abnormal, CS	Normal	Abnormal, NCS	Abnormal, CS	Normal	Abnormal, NCS	Abnormal, CS
Visit Result	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)	nn n (%)
DAY 1 (Pre-dose) Normal	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)
Abnormal, NCS	xx(xx.x)	xx(xx.x)	xx (xx.x)	xx(xx.x)	xx (xx.x)	xx (xx.x)	xx(xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Abnormal, CS	xx(xx.x)	xx (xx.x)	xx (xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
DAY 1 (8 HOURS POSTDOSE) Normal	nn xx(xx.x)	nn xx (xx.x)	nn xx (xx.x)	nn xx(xx.x)	nn xx (xx.x)	nn xx (xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx(xx.x)	nn xx (xx.x)	nn xx(xx.x)	nn xx(xx.x)
Abnormal, NCS	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Abnormal, CS	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)	xx(xx.x)
Etc.												

AB_F05
VIS_F01

EG_F02 (for Parts A and B) or EG_F01D for Part D
EG_F01

Listing Source: EG_LAA_F_X

Notes:

1) ***Include all visits where ECGs were scheduled per the protocol.***
2) ***Only subjects with non-missing values at baseline and the post-baseline visit are included in the denominators for the percentages.***

Chest X-Ray

Non-unique tables for EG_TAA_F_X:

Table 14.3.7.1 (CX_TAA_F_X)
Shift in Chest X-Ray by Visit and Dose Group
Population: Safety Analysis Set

AB_F05
VIS_F01
BL_F01
XR_F01

Listing Source: CX_LAA_F_X

Notes:

1) ***Include all visits where chest x-ray was scheduled per the protocol.***
2) ***Only subjects with non-missing values at baseline and the post-baseline visit are included in the denominators for the percentages.***

Physical Examination

Table 14.3.8.1 (PE_TAA_F_X)
Summary of Physical Examination by Visit and Dose Group
Population: Safety Analysis Set

Part: x Parameter Visit Result	MRT5005 Xmg N=xx n/nn (%)	MRT5005 Xmg N=xx n/nn (%)	MRT5005 Xmg N=xx n/nn (%)	Pooled Placebo N=xx n/nn (%)
General Appearance				
Baseline				
Normal	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
Abnormal, Not Clinically Significant	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
Abnormal, Clinically Significant	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
DAY 1				
Normal	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
Abnormal, Not Clinically Significant	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
Abnormal, Clinically Significant	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)	xx/xx (xx.x)
Etc.				

BL_F01S (for Parts A and B); BL_F01P (for Part D)
VIS_F01a

Listing Source: PE_LAA_F_X

Notes:

1) ***Include all visits where physical examination was done.***
2) ***Include all physical examination parameters***
3) ***Only subject with non-missing values at each visit are included in the denominators for the percentages.***
4) ***For Part D, label Screening as Baseline***

Spirometry

Table 14.3.9.1 (RE_TAA_F_X)
Mean and Mean Absolute Change from Baseline in Spirometry Values by Visit and Dose Group
Population: Safety Analysis Set

Part: x Parameter (unit) Visit Statistic	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	MRT5005 Xmg N=xx Actual	 Absolute Change from Baseline	Pooled Placebo N=xx Actual	 Absolute Change from Baseline
Parameter 1 (unit)								
Baseline [1]								
Subject 1	xx		xx		xx		xx.x	
Subject 2	xx		xx		xx		xx.xx	
Subject 3	xx		xx		xx		xx	
Subject 4	xx		xx		xx		xx	
Mean	xx.x		xx.x		xx.x		xx	
SD	xx.xx		xx.xx		xx.xx		xx	
SE	xx.xx		xx.xx		xx.xx		xx	
Day 1 (8 HOURS POSTDOSE)								
Subject 1	xx	xx	xx	xx	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
SE	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Etc.								

AB_F01
[1] RE_F01 (Parts A and B) and RE_F01D (Part D)
CH_F01

Listing Source: RE_LAA_F_X

Notes:

1) ***Parameters include: FEV1, Percent Predicted FEV1, FVC, Percent Predicted FVC, FEV1/FVC, $FEF_{25-75\%}$, PEF***
2) ***Include all planned (per the protocol) post-baseline visits/timepoints where spirometry is performed and collected.***

Non-unique tables for RE_TAA_F_X:

Table 14.3.9.2 (RE_TAB_F_X)
Mean and Mean Relative Change from Baseline in Spirometry Values by Visit and Dose Group
Population: Safety Analysis Set

AB_F01
[1] RE_F01 (Parts A and B) and RE_F01D (Part D)
CH_F02

Listing Source: RE_LAA_F_X

Notes:

1) ***Repeat table RE_TAA_F_X and summarize relative change from baseline rather than absolute change from baseline.***
2) ***Replace "Absolute" in column headers with "Relative".***

Concomitant Medications

Table 14.3.10.1 (CM_TAA_F_X)
Number and Percentage of Subjects with Concomitant Medications by Anatomic Class, Therapeutic Class, Medication Term, and Dose Group
Population: Safety Analysis Set

Part: x Anatomic Class Therapeutic Class Medication Term	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	MRT5005 Xmg N=xx n (%)	Total N=xx n (%)
Any Concomitant Medication	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Anatomic Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Therapeutic Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medication Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medication Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Anatomic Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Therapeutic Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medication Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Medication Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.				

CM_F01
CM_F02
CM_F03
CM_F04
CM_F05
CM_F06
CM_F08

Listing Source: CM_LAA_F_X

Notes:

1) ***CM_TAA_F_X will be produced for each study part and for the study overall.***
2) ***Sort Anatomic Class, Therapeutic Class, and Medication Terms within by descending order of overall (MRT5005 + Placebo) frequency.***

Non-unique tables for CM_TAA_F_X:

Table 14.3.10.2 (CM_TAB_F_X)
Number and Percentage of Subjects with Prior Medications by Anatomic Class, Therapeutic Class, Medication Term, and Dose Group
Population: Safety Analysis Set

CM_F01
CM_F02
CM_F03
CM_F04
CM_F05
CM_F07
CM_F08

Listing Source: CM_LAA_F_X

Notes:

1) ***CM_TAB_X will be produced for each study part and for the study overall.***
2) ***Sort Anatomic Class, Therapeutic Class, and Medication Terms within by descending order of overall (MRT5005 + Placebo) frequency.***

CFQ-R

Table 14.4.1 (QS_TAA_F_B)
Mean and Mean Change from Baseline in CFQ-R Respiratory Domain Scores by Visit and Dose Group
Population: Safety Analysis Set

Part: x	MRT5005 Xmg N=xx		MRT5005 Xmg N=xx		MRT5005 Xmg N=xx		Pooled Placebo N=xx	
Visit Statistic	Actual	Absolute Change from Baseline	Actual	Absolute Change from Baseline	Actual	Absolute Change from Baseline	Actual	Absolute Change from Baseline
Baseline								
Subject 1	xx		xx		xx		xx	
Subject 2	xx		xx		xx		xx	
Subject 3	xx		xx		xx		xx	
Subject 4	xx		xx		xx		xx	
Mean	xx.x		xx.x		xx.x		xx.x	
SD	xx.xx		xx.xx		xx.xx		xx.xx	
Day 36								
Subject 1	xx	xx	xx	xx	xx	xx	xx	xx
Subject 2	xx	xx	xx	xx	xx	xx	xx	xx
Subject 3	xx	xx	xx	xx	xx	xx	xx	xx
Subject 4	xx	xx	xx	xx	xx	xx	xx	xx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Etc.								

AB_F06
CH_F01
CFQ_F01
CFQCH_F01

Listing Source: QS_LAA_F_X

Notes:

1) Include Baseline (Day -1) and Days 36, 43, 57, 85, 113, 281, and 365.

Footnotes

Data Type	Footnote Type	Code	Prefix	Footnote
All	Percent	PC_F02	Note:	Percentages were based on the number of subjects (N) in the population analyzed.
All	Baseline	BL_F01	Note:	Baseline was defined as the last measurement taken prior to the first dose, obtained on or prior to the day of first dose of study drug.
All	Baseline	BL_F01P	Note:	Baseline was defined as the Screening measurement.
All	Baseline	BL_F01S	Note:	Baseline was defined as the Day -1 complete physical exam.
All	Change from Baseline	CH_F01	Note:	Change from baseline was defined as visit value – baseline value.
All	Change from Baseline	CH_F02	Note:	Relative change from baseline was defined as (visit value – baseline value)/(baseline value)*100.
All	By Visit	VIS_F01		n = Number of subjects with the specified result at the specified visit and non-missing baseline result; nn = Number of subjects with a non-missing result at the specified visit; (%) = Percentage of subjects with the specified result at the specified visit.
All	By Visit	VIS_F01a		n = Number of subjects with the specified result at the specified visit; nn = Number of subjects with a non-missing result at the specified visit; (%) = Percentage of subjects with the specified result at the specified visit.
All	Abbreviation	AB_F01		SD = standard deviation; SE = standard error
All	Abbreviation	AB_F01a		SD = standard deviation
All	Abbreviation	AB_F02		CFTR = cystic fibrosis transmembrane conductance regulator; FEV_1 = forced expiratory volume in 1 second; SD = standard deviation
All	Abbreviation	AB_F03		AE = adverse event; IP = investigational product; TEAE = treatment-emergent adverse event
All	Abbreviation	AB_F04		AE = adverse event; TEAE = treatment-emergent adverse event
All	Abbreviation	AB_F05		CS = clinically significant; ECG = electrocardiogram; NCS = not clinically significant
All	Abbreviation	AB_F06		CFQ-R = Cystic fibrosis questionnaire-revised; SD = standard deviation; SE = standard error
DS	Percent	DS_F03	[2]	The denominator was defined as the total number of subjects who discontinued the study.
DM	Age	DM_F01	[1]	Age was calculated by (date of informed consent - date of birth)/365.25, rounded down to the next largest integer using the floor function, in years.

Data Type	Footnote Type	Code	Prefix	Footnote
DM	CFTR	DM_F02	[2]	CFTR Modulator use at baseline was defined as a concomitant CFTR modulator that was in use at the start of treatment, or a CFTR modulator with missing start date.
CM	Percent	CM_F01	Note:	n = Number of subjects that reported at least 1 medication within an Anatomic Class, Therapeutic Class, and Medication Term; (%) = Percentage of subjects among the population analyzed (N).
CM	Count	CM_F02	Note:	A subject that reported more than 1 medication for a particular Anatomic Class was counted only once for each Anatomic Class.
CM	Count	CM_F03	Note:	A subject that reported more than 1 medication for a particular Therapeutic Class was counted only once for each Therapeutic Class.
CM	Count	CM_F04	Note:	A subject that reported more than 1 medication for a particular Medication Term was counted only once for each Medication Term.
CM	Order	CM_F05	Note:	Medications were presented in order of decreasing frequency, by Anatomic Class, Therapeutic Class, and Medication Term.
CM	Definition	CM_F06	Note:	Concomitant medications included all medications in use at date of first study drug dose or started after date of first study drug dose, any medications that started prior to the day of first dose of study drug with missing stop date, any medications with missing start and stop dates or were classified as ongoing.
CM	Definition	CM_F07	Note:	Prior medications included all medications that stopped prior to the day of first dose of the study drug, medications that started prior to the day of first dose of study drug with missing stop date or medications with missing start and stop dates.
CM	Dictionary	CM_F08	Note:	Anatomic Class, Therapeutic Class, and Medication Term were based on the WHO Drug Global (2020-SEP) coding dictionary.
MH	Count	MH_F01	Note:	If a subject had more than 1 medical history event within a system organ class, the subject was counted only once in that system organ class. If a subject had more than 1 medical history event that coded to the same preferred term, the subject was counted only once for that preferred term.
AE	Count	AE_F05	[1]	Subjects that experienced 1 or more adverse events were counted once.
AE	Count	AE_F06a	[2]	If a subject experienced more than 1 adverse event, the subject was counted only once for the closest relationship to IP. AEs with missing relationships to IP were classified as being Related to IP.
AE	Count	AE_F06b	[3]	If a subject experienced more than 1 adverse event, the subject was counted only once for the closest relationship to nebulization/treatment administration. AEs with missing relationships were classified as being Related to nebulization/treatment administration.

Data Type	Footnote Type	Code	Prefix	Footnote
AE	Count	AE_F06d	[5]	If a subject experienced more than 1 adverse event classified as a pulmonary exacerbation, the subject was only counted once in the 'All' row. Subjects with both an investigator-defined and a protocol-defined TEAE classified as a pulmonary exacerbation were counted once in each row, 'Investigator-Defined' and 'Protocol-Defined'.
AE	Count	AE_F07	[4]	If a subject experienced more than 1 adverse event, the subject was counted only once for the maximum severity. AEs with missing severities were counted as Severe.
AE	Count	AE_F07a	[2]	If a subject experienced more than 1 adverse event with a preferred term associated with the febrile reaction, the subject was counted only once for the maximum severity of any of the preferred terms contributing to the febrile reaction. AEs with missing severity were counted as Severe.
AE	Count	AE_F07b	[2]	If a subject experienced more than 1 hypersensitivity reaction, the subject was counted only once for the maximum severity of any of the hypersensitivity reactions. AEs with missing severity were counted as Severe.
AE	Order	AE_F08	Note:	Incidences were displayed in descending order of frequency of System Organ Class and by Preferred Term within System Organ Class.
AE	Order	AE_F09	Note:	Incidences were displayed in descending order of frequency of Preferred Term.
AE	Dictionary	AE_F14	Note:	System Organ Class and Preferred Term were based on the Version 23.1 of the MedDRA coding dictionary.
AE	Dictionary	AE_F14a	Note:	Preferred Term was based on the Version 23.1 of the MedDRA coding dictionary.
AE	Interval	AE_F15	Note:	Time intervals were determined by the start day of the adverse event.
AE	Count	AE_F16	Note:	n represents the number of subjects that experienced an adverse event in a given category. m represents the number of adverse events in a given category.
AE	Definition	AE_F17a	Note:	Febrile reactions were identified based on a preferred term of body temperature increased or preferred term of pyrexia within the 24 hours after completion of nebulization on any dosing day with at least one other systemic symptom reported as a preferred term of headache, arthralgia, myalgia, fatigue, chills, nausea, or vomiting within the 24 hours after completion of nebulization on any dosing day.
AE	Definition	AE_F17b	Note:	Hypersensitivity reactions were identified based on a preferred term of hypersensitivity within the 24 hours after completion of nebulization on any dosing day.
AE	Definition	AE_F17c	[2]	Severity grade for each febrile reaction was based on the maximum severity of the preferred terms comprising the febrile reaction. Febrile reactions with missing severity were counted as Severe.

Data Type	Footnote Type	Code	Prefix	Footnote
AE	Interval	AE_F18	Note:	The 1 month post-dose time interval is defined as through Day 29 for Part A, through Day 57 for Part B, through Day 32 for Part D.
AE	Count	AE_F19	Note:	N represents the number of subjects in a given dose group that experienced an adverse event.
EG	Baseline	EG_F01	Note:	The baseline value was defined as the Day -1 ECG measurement.
EG	Baseline	EG_F01D	Note:	The baseline value was defined as the screening ECG measurement.
EG	Schedule	EG_F02	Note:	Only ECGs scheduled per the protocol were summarized.
EX	Count	EX_F01	Note:	Full dose refers to completion of all nebulizers as planned; partial dose refers to incomplete nebulization. Full and partial dose are independent of the presence or absence of excess residual in the medication chamber.
VS	Schedule	VS_F01	Note:	The final recording during nebulization for blood pressure, pulse rate, and pulse oximetry was counted as the 'DAY 1 (0 HR POST-DOSE)' value.
RE	Baseline	RE_F01	[1], [3]	The baseline value was defined as the average of the results from testing on Day -1 and at pre-dose on Day 1.
RE	Baseline	RE_F01D	[1],[3]	The baseline value was defined as the result from testing pre-dose on Day 1.
RE	Baseline	RE_F01O	[1],[3]	The baseline value was defined as the average of the results from testing on Day -1 and at pre-dose on Day 1 for Part A and Part B, and defined as the result from testing pre-dose on Day 1 for Part D.
CFQ	Baseline	CFQ_F01	Note:	The baseline value was defined as the Day -1 CFQ-R respiratory domain score.
CFQ	Baseline	CFQCH_F01	Note:	At baseline, all subjects with baseline data contributed to the reported baseline mean. For each visit, the mean actual value was the mean across all subjects with data at that visit. The change from baseline was calculated for each subject with data at baseline and that visit, then reported as a mean change.
XR	Schedule	XR_F01	Note:	Only chest x-rays scheduled per the protocol were summarized.

Translate Bio, Inc.
PROTOCOL NUMBER MRT5005-101

A Phase 1/2, Randomized, Double-Blind, Placebo-Controlled, Combined Single and Multiple Ascending Dose Study Evaluating the Safety, Tolerability, and Biological Activity of MRT5005 ([redacted] mRNA/[redacted] LNP) Administered by Nebulization to Adult [redacted] with [redacted] ic Fibrosis

Listing Specifications

VERSION DATE: 26 October 2021

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Listing Specifications

Table of Contents

General Programming Notes

The following instructions apply to all listing displays.

DISPLAY OUTPUTS FOR EACH PART
Each listing will be produced for each study part (A, B, D), unless otherwise specified. Listings will not be produced for the study overall. Each version of the listing will include the relevant study part in the header and in the listing identifier. For example, DS_LAA_F_X will be identified as DS_LAA_F_A for Part A and will include a header to show 'Part A'. A, B or D will be added to each display number.

PROGRAMMER NOTES

Programmer notes appear at the bottom of each listing display shell where applicable.

Dose groups for each part are as follow:

- Part A: MRT5005 8mg, MRT5005 16mg, MRT5005 20mg, MRT5005 24mg, Pooled Placebo
- Part B: MRT5005 8mg, MRT5005 12mg, MRT5005 16mg, MRT5005 20mg, Pooled Placebo
- Part D: MRT5005 4mg, Placebo

The maximum number of decimal places reported will be 4.

PAGE FORMATTING

The specifications for the format of each page are page size=47, line size=134, font=Courier, font size=8, and margin = 1.5" top, 1" bottom, left, and right.

"Dataset Source: <Dataset Name>" will be printed on the right side of the footer for each listing.

SORTING

Unless otherwise specified, listings are sorted by Subject Number, Visit Number, in that order when the variables are included in the table. Only show the value of a sort-variable when it changes or when a new page starts. Insert a blank row between the data for subjects.

Listing 16.2.1.1 (DS_LAA_F_X)
Listing of Screen Failures
Population: Screened Subjects

Part: x

Subject Number	Date of Informed Consent	Date of Screen Failure	Reason for Screen Failure/Other, Specify
XXXX	YYYY-MM-DD	YYYY-MM-DD	XXXXXXX/XXXXX
XXXX	YYYY-MM-DD	YYYY-MM-DD	XXXXXXX/XXXXX
Etc.			

Dataset Source: ADSL

Listing 16.2.1.2 (DS_LAB_F_X)
Listing of Subject Disposition
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Date of Informed Consent	Date of Randomization/ Date of First Dose of Study Drug	Date of Last Dose of Study Drug/ Study Day [1]	Did subject receive all study treatment?	Date of Completion or Early Termination/ Study Day [2]	Completed the study?	Reason for Study Withdrawal/Other, Specify
XXXX	YYYY-MM-DD	YYYY-MM-DD/ YYYY-MM-DD	YYYY-MM-DD/ XX	Yes	YYYY-MM-DD/ XX	Yes	XXXXXXX/ XXXXX
XXXX	YYYY-MM-DD	YYYY-MM-DD/ YYYY-MM-DD	YYYY-MM-DD/ XX	No	YYYY-MM-DD/ XX	No	XXXXXXX/ XXXXXXXX
Etc.							

[1] DS_L01
[2] DS_L02

Dataset Source: ADSL

Notes:

1) Dose groups are specified in the general programming notes.

Listing 16.2.1.3 (DS_LAC_F_X)
Listing of Visits Not Done, Conducted as Home Health Visits, or Visits Conducted as Telephone Visits as a Replacement for a Scheduled In-Clinic Visit
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Visit Date	Visit Not Done or Visit Type	Reason
XXXX	XXXXXXXX	YYYY-MM-DD	XXXXXX	XXXXXXXXXXXXXX XXXXXXXXXXXXXX
XXXX	XXXXXXXX	YYYY-MM-DD	XXXXXX	XXXXXXXXXXXXXX XXXXXXXXXXXXXX
Etc.				

Dataset Source: VE, SUPPVE

Notes:

1) ***Dose groups are specified in the general programming notes.***
2) ***List any visits not done, conducted as home health visit, or visit conducted as a telephone visit as a replacement for a scheduled in-clinic visit.***

Listing 16.2.2 (PD_LAA_F_X)
Listing of Protocol Deviations
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Date Deviation was Discovered	Associated Study Visit/ Date Deviation Started	Protocol Deviation Type/ Protocol Deviation Description	Corrective/Preventative Action	Reportable to the IRB?/ Date IRB Notified
XXXX	YYYY-MM-DD	XXXXXX/ YYYY-MM-DD	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	XXXXXXXXXXXXXX	No/
XXXX	YYYY-MM-DD	XXXXXX/ YYYY-MM-DD	XXXXXXXXXXXXXX/ XXXXXXXXXXXXXX	XXXXXXXXXXXXXX	Yes/ YYYY-MM-DD
Etc.					

Dataset Source: DV, SUPPDV

Notes:

1) ***Dose groups are specified in the general programming notes.***
2) ***Listing will include both blinded and unblinded protocol deviations***

Listing 16.2.4.1 (DM_LAB_F_X)
Listing of Demographics and Baseline Characteristics
Population: Safety Analysis Set

Part: x
Dose Group: xx

								Genotype	
Subject Number	Date of Randomization	Date of Birth	Age [1]	Sex	Race/ Ethnicity	CFTR Modulator Use	Baseline Percent Predicted FEV_1 [2]	First Mutation Class/Second Mutation Class	First Mutation Name/Second Mutation Name
XXXX	YYYY-MM-DD	YYYY-MM-DD	XX	Male	White/ Hispanic or Latino	Yes	XX.X	XXX/XXX	XXX/XXX
XXXX	YYYY-MM-DD	YYYY-MM-DD	XX	Female	Other: XXXXXXXXXX/ Not Hispanic or Latino	No	XX.X	XXX/XXX	XXX/XXX
Etc.									

DM_L02
[1] DM_L01
[2] RE_L02

Dataset Source: ADSL

Notes:
1) Dose groups are specified in the general programming notes.

Listing 16.2.5.1 (EX_LAB_F_B, EX_LAB_F_D)
Listing of Overall Extent of Exposure
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Number of Full Doses Administered	Number of Partial Doses Administered
XXXX	xx	xx
XXXX	xx	xx
Etc.		

Note: EX_F01

Dataset Source: ADEXSUM

Notes:
1) Dose groups are specified in the general programming notes.

Listing 16.2.5.2 (EX_LAC_F_X)
Listing of Extent of Exposure at the Visit Level
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of IP Administration /Study Day	Was Full Dose Administered?	Reason Full Dose Was Not Administered	Actual Number of Medication Chambers Completed/ Expected Number of Medication Chambers Completed
XXXX		YYYY-MM-DD/ XX	Yes		xx/xx
XXXX		YYYY-MM-DD/ XX	No	xxxxxxx	xx
XXXX		YYYY-MM-DD/ XX	Yes		xx
Etc.					

Note: EX_L01
Note: EX_L02
Note: EX_F01

Dataset Source: ADEXVIS

Listing 16.2.5.3 (EX_LAA_F_X)
Listing of Investigational Product Administration
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Start Date/Time of Nebulizer/ Study Day	End Date/Time of Nebulizer/ Study Day	Nebulization Complete	Excess Residual in Medication Chamber?
XXXX		YYYY-MM-DD/ XX	YYYY-MM-DD/ XX	Yes	No
		YYYY-MM-DD/ XX	YYYY-MM-DD/ XX	Yes	No
		YYYY-MM-DD/ XX	YYYY-MM-DD/ XX	No	Yes
XXXX		YYYY-MM-DD/ XX	YYYY-MM-DD/ XX	Yes	No
Etc.					

Note: EX_F01

Dataset Source: ADEX

Notes:

1) ***Dose groups are specified in the general programming notes.***
2) ***Remove fully missing records.***

Listing 16.2.6.1 (MH_LAA_F_X)
Listing of Medical History by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	System Organ Class/ Preferred Term	Medical History Event	Start Date/ Study Day	End Date/ Study Day	Ongoing?
XXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	XXXXXXXXXXXXXXX	YYYY-MM-DD/ XX	YYYY-MM-DD/ XX	No
		…			
XXXX	XXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXX	XXXXXXXXXXXXX	YYYY-MM-DD/ XX		Yes
Etc.					

Note: AE_L03

Dataset Source: ADMH

Notes:

1.) Sort by Dose Group, Subject Number, Start Date, Stop Date, System Organ Class, Preferred Term.

2.) Dose groups are specified in the general programming notes.

Listing 16.2.7.1 (AE_LAA_F_X)
Listing of Adverse Events by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Start Date/Start Time/Study Day End Date/ End Time/ Study Day/ Ongoing?	System Organ Class/ Preferred Term/ Verbatim Term	AE Duration (days)	Severity/ Action Taken	Outcome/ Specify	Relationship to IP	Relationship to Nebulization/ Treatment Administration	Serious AE?	Treatment-Emergent?
XXXX	YYYY-MM-DD/HH:MM:SS / XX/ YYYY-MM-DD/ HH:MM:SS/XX / No	XXXXXXXXXXXX XXX/ XXXXXXXXXXXX XXX/ XXXXXXXXXXXX XXXX …	XX	XXXXXX/ XXXXXX	XXXXXX/	XXXXXXXX X	XXXXXXXXX	Yes	Yes
XXXX	YYYY-MM-DD/ HH:MM:SS/XX / YYYY-MM-DD/ HH:MM:SS/XX / No	XXXXXXXXXXXX XXX/ XXXXXXXXXXXX XXX/ XXXXXXXXXXXX XXXX	XX	XXXXXX/ XXXXXX	XXXXXX/ XXXX	XXXXXXXX X	XXXXXXXXX	No	No
Etc.									

Note: AE_L01
Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Notes:
1.) Sort by Dose Group, Subject Number, Start Date, Stop Date, System Organ Class, Preferred Term, Verbatim Term.
2.) Dose groups are specified in the general programming notes.

Non-unique listings for (for AE_LAA):

Listing 16.2.7.2 (AE_LAB_F_X)
Listing of Adverse Events Leading to Treatment Discontinuation by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Note: AE_L01
Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Listing 16.2.7.3 (AE_LAD_F_X)
Listing of Adverse Events Resulting in Death by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Note: AE_L01
Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Listing 16.2.7.4 (AE_LAC_F_X)
Listing of Serious Adverse Events by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Note: AE_L01
Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Listing 16.2.7.5 (AE_LAL_F_X)
Listing ofAdverse Events of Special Interest by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Note: AE_L01
Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Listing 16.2.7.6 (AE_LAF_F_X)
Listing of Adverse Events Classified as Pulmonary Exacerbations (Investigator and Protocol-Defined) by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Note: AE_L01

Note: AE_L02
Note: AE_L03

Dataset Source: ADAE

Notes:
1.) Add "Type" to the Treatment Emergent column with values of "Investigator-Defined" and "Protocol-Defined".

Listing 16.2.7.7 (AE_LAI_F_X)
Listing of Pyrexia or Elevated Body Temperature Adverse Events Reported During and Up To 24 Hours After Completion of Nebulization by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Start Date/Start Time/Study Day End Date/ End Time/ Study Day/ Ongoing?	Start Time Relative to End of Nebulization (Hours) [1]	System Organ Class/ Preferred Term/ Verbatim Term	Severity/ Action Taken	Outcome/ Specify	Relationship to IP	Relationship to Nebulization/ Treatment Administration	Serious AE?
XXXX	YYYY-MM-DD/HH:MM:SS / XX/ YYYY-MM-DD/ HH:MM:SS/XX / No	XX	XXXXXXXXXXXX XXX/ XXXXXXXXXX/ XXXXXXXXXXX	XXXXXX/ XXXXXX	XXXXXX/	XXXXXXXX X	XXXXXXXXX	Yes
		…	…					
XXXX	YYYY-MM-DD/ HH:MM:SS/XX / YYYY-MM-DD/ HH:MM:SS/XX / No	N/A (During)	XXXXXXXXXXX XXX XXXXXXXXXX/ XXXXXXXXXXX	XXXXXX/ XXXXXX	XXXXXX/ XXXX	XXXXXXXX X	XXXXXXXXX	No
Etc.								

[1] AE_L06
Note: AE_L01
Note: AE_L03
Note: AE_L04

Dataset Source: ADAE

Notes:
1.) Sort by Dose Group, Subject Number, Start Date, Stop Date, System Organ Class, Preferred Term, Verbatim Term.
2.) Dose groups are specified in the general programming notes.

3.) For any subject with an AE of Pyrexia or Elevated Body Temperature within 24 hours after dosing, include all other AEs for that subject that occurred within 24 hours after dosing.
4.) Add footnote reference [1] to column 3.
5.) Round start time relative to end of nebulization (hours) to 2 decimal places.

Listing 16.2.7.8 (AE_LAJ_F_X)
Listing of Adverse Events Reported During and Up To 24 Hours After Completion of Nebulization by Subject, System Organ Class, and Preferred Term
Population: Safety Analysis Set

[1] AE_L06
Note: AE_L01
Note: AE_L03

Dataset Source: ADAE

Notes:
1.) Sort by Dose Group, Subject Number, Start Date, Stop Date, System Organ Class, Preferred Term, Verbatim Term.
2.) Dose groups are specified in the general programming notes.
3.) Include any AE that occurred during nebulization or within 24 hours after dosing.
4.) Add footnote reference [1] to column 3.
5.) Round start time relative to end of nebulization (hours) to 2 decimal places.

Listing 16.2.7.9 (AE_LAK_F_X)
Listing of Febrile Reactions and Hypersensitivity Reactions in First 24 Hours After Completion of Nebulization by Subject and Preferred Term
Population: Safety Analysis Set

[1] AE_L08
Note: AE_L01
Note: AE_L03

Dataset Source: ADAE

Notes:
1.) Sort by Dose Group, Subject Number, Start Date, Stop Date, System Organ Class, Preferred Term, Verbatim Term.
2.) Dose groups are specified in the general programming notes.
3.) For any subject with a febrile reaction or hypersensitivity reaction during or within 24 hours after dosing, include all other AEs that meet the criteria for febrile reaction or hypersensitivity reaction for that subject that occurred during nebulization or within 24 hours after dosing.
4.) Add footnote reference [1] to column 3.

Listing 16.2.8.1 (LB_LAA_F_X)
Listing of Chemistry Values
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date/Time of Assessment/ Study Day	Lab Test (units)	Result	Classification/ CS?/ Comment	Reference Range
XXXX		YYYY-MM-DD/HH:MM:SS	Albumin	XXX		
			Alkaline Phosphatase	XXX		
			ALT	XXX		
			AST	XXX		
			Blood Urea Nitrogen	XXX		
		YYYY-MM-DD/HH:MM:SS	…	XXX		
		YYYY-MM-DD/HH:MM:SS	…	XXX		
XXXX		YYYY-MM-DD/HH:MM:SS		XXX		
Etc.						

CS_01
Note: LB_01

Dataset Source: ADLB

Notes:

1) Laboratory parameters are listed alphabetically.
2) Dose groups are specified in the general programming notes.

Non-unique listings for LB_LAA:

Listing 16.2.8.2 (LB_LAB_F_X)
Listing of Hematology Values
Population: Safety Analysis Set

CS_01
Note: LB_01

Dataset Source: ADLB

Listing 16.2.8.3 (LB_LAC_F_X)
Listing of Urinalysis Values
Population: Safety Analysis Set

CS_01
Note: LB_01

Dataset Source: ADLB

Listing 16.2.8.4 (LB_LAD_F_B, LB_LAD_F_D)
Listing of Coagulation Values
Population: Safety Analysis Set

CS_01
Note: LB_01

Dataset Source: ADLB

Listing 16.2.8.5 (LB_LAE_F_B, LB_LAE_F_D)
Listing of Serum Inflammatory Markers
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date/Time of Assessment/ Study Day	Marker	Result	Reference Range
XXXX		YYYY-MM-DD/HH:MM:SS	Interferon	XXX	
			Interleukin-1B	XXX	
			Interleukin-2	XXX	
			Interleukin-4	XXX	
			Interleukin-6	XXX	
			Interleukin-8	XXX	
			Interleukin-10	XXX	
			Interleukin-12p70	XXX	
			Interleukin-13	XXX	
			Tumor Necrosis Factor	XXX	
		YYYY-MM-DD/HH:MM:SS	…	XXX	
		YYYY-MM-DD/HH:MM:SS	…	XXX	
XXXX		YYYY-MM-DD/HH:MM:SS		XXX	
Etc.					

Dataset Source: ADLB

Notes:

1) Inflammatory markers are listed alphabetically.

2) Dose groups are specified in the general programming notes.

Listing 16.2.8.8 (PG_LAA_F_X)
Listing of Pregnancy Results
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of Assessment/ Study Day	Was the Pregnancy Test Completed?	Pregnancy Test Result
XXXX		YYYY-MM-DD/XX	Yes	Negative
		YYYY-MM-DD/XX	Yes	Negative
XXXX		YYYY-MM-DD/XX	Yes	Negative
Etc.				

Dataset Source: ADLB

Listing 16.2.9.1 (VS_LAA_F_X)
Listing of Vital Signs
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit/ Timepoint	Visit Date/Time/ Study Day	Systolic Blood Pressure (mmHg)/ Diastolic Blood Pressure (mmHg)	Pulse Rate (bpm)	Respiratory Rate (breaths/min)	Temperature (C)	Pulse Oximetry (%)	Weight (kg)
XXXX		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
XXXX		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
		YYYY-MM-DD/HH:MM:SS						
Etc.								

Dataset Source: ADVS

Listing 16.2.10.1 (EG_LAA_F_X)
Listing of Overall Electrocardiogram Interpretation Findings
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of Assessment/ Study Day	Result
XXXX		YYYY-MM-DD/ XX	
		YYYY-MM-DD/ XX	
		YYYY-MM-DD/ XX	
XXXX		YYYY-MM-DD/ XX	
Etc.			

CS_01

Dataset Source: ADEG

Listing 16.2.11.1 (CX_LAA_F_X)
Listing of Chest X-Ray Findings
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of Assessment/ Study Day	Result	Details
XXXX		YYYY-MM-DD/ XX		
		YYYY-MM-DD/ XX		
		YYYY-MM-DD/ XX		
XXXX		YYYY-MM-DD/ XX		
Etc.				

CS_01

Dataset Source: ADCX

Listing 16.2.12.1 (PE_LAA_F_X)
Listing of Physical Examination Results
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of Assessment/ Study Day	Body System Examined	Result	Description
XXXX		YYYY-MM-DD/ XX	General Appearance	xxxxxxx	xxxxxxx
			Skin	xxxxxxx	xxxxxxx
			Etc.		
		YYYY-MM-DD/ XX			
XXXX		YYYY-MM-DD/ XX			
Etc.					

CS_01
PE_L01

Dataset Source: ADPE

Listing 16.2.13.1 (RE_LAA_F_X)
Listing of Spirometry Values
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date/Time of Assessment/ Study Day	Spirometry Test [1]	Result	Reference Result
XXXX		YYYY-MM-DD/HH:MM:SS/ XX	FEF2575	XXX	
			FET	XXX	
			FEV1	XXX	
			FEV1FVC		
		YYYY-MM-DD/HH:MM:SS/ XX	…	XXX	
		YYYY-MM-DD/HH:MM:SS/ XX	…	XXX	
XXXX		YYYY-MM-DD/HH:MM:SS/ XX		XXX	
Etc.					

[1] RE_L01
Note: RE_L02
Note: RE_L03

Dataset Source: ADRE

Notes:
1) For RE_LAA_D, remove footnote RE_L02.
2) Present Baseline-Derived after Day 1 (pre-dose)

Listing 16.2.14.1 (CM_LAA_F_X)
Listing of Prior and Concomitant Medications
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Anatomic Class/ Therapeutic Class/ Preferred Name/ Verbatim Term	Start Date(Study Day)/ Stop Date (Study Day)/ Ongoing?	Prior or Concomitant?	Dose/ Unit/ Dose Form	Indication	Route/ Frequency	Taken for AE?
XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ Yes	Concomitant	XXX/ XXX/ XXX	XXXXXXXXX	XXXXXXXXX/ XXXX	Yes
	XXXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ YYYY-MM-DD	Prior	XXX/ XXX/ XXX	XXXXXXXXX	XXXXXXXXX/ XXXX	
XXXX	XXXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ YYYY-MM-DD	Concomitant	XXX/ XXX/ XXX	XXXXXXXXX	XXXXXXXXX/ XXXX	No
	XXXXXXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD	Concomitant	XXX/ XXX/ XXX	XXXXXXXXX	XXXXXXXXX/ XXXX	No

Note: CM_L01
Note: CM_L02

Dataset Source: ADCM

Listing 16.2.14.2 (CM_LAB_F_X)
Listing of Concomitant Surgical Procedures
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	System Organ Class/ Preferred Term/ Procedure	Start Date (Study Day)/ Stop Date (Study Day)	Indication
XXXX	XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	YYYY-MM-DD (XX)/ YYYY-MM-DD (XX)	XXXXXXXXX
	XXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	YYYY-MM-DD (XX)/ YYYY-MM-DD (XX)	XXXXXXXXX
XXXX	XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXX	YYYY-MM-DD (XX)/ YYYY-MM-DD (XX)	XXXXXXXXX

Note: AE_L03

Dataset Source: PR

Listing 16.2.15.1 (QS_LAA_F_B)
Listing of CFQ-R Respiratory Domain Scores
Population: Safety Analysis Set

Part: x
Dose Group: xxx

Subject Number	Visit	Date of Assessment/ Study Day	Question	Response
XXXX	XXXXXXX	YYYY-MM-DD/ XX	XXXXXXXXXXXXXXXXXXXXXXXXX	XXX
			XXXXXXXXXXXXXXXXXXXXXXXXX	XXX
			Respiratory Domain Score	XXX
XXXX	XXXXXXX	YYYY-MM-DD/ XX	XXXXXXXXXXXXXXXXXXXXXXXXX	XXX
			XXXXXXXXXXXXXXXXXXXXXXXXX	XXX
			Respiratory Domain Score	XXX

QS_F01

Dataset Source: ADQS

Notes:

1) Include questions that contribute to the respiratory domain score.
2) Include all visits (Baseline and Days 36, 43, 57, 85, 113, 197, 281, 365).

Footnotes

Data Type	Footnote Type	Code	Prefix	Footnote
DS	Study day	DS_L01	[1]	Study day of last dose of study drug was defined as treatment end date – treatment start date + 1.
DS	Study day	DS_L02	[2]	Study day was defined as date of completion or early termination – treatment start date + 1.
DM	Derivation	DM_L01	[1]	Age is calculated by (date of informed consent - date of birth)/365.25, rounded down to the next largest integer using the floor function, in years.
DM	Abbreviation	DM_L02		CFTR = cystic fibrosis transmembrane conductance regulator.
EX	Schedule	EX_L01	Note:	For the 4 mg dose group, 1 medication chamber was expected. For the 8 mg dose group, 2 medication chambers were expected. For the 12 mg dose group, 3 medication chambers were expected. For the 16 mg dose group, 4 medication chambers were expected. For the 20 mg dose group, 5 medication chambers were expected. For the 24 mg dose group, 6 medication chambers were expected.
EX	Derivation	EX_L02	Note:	A medication chamber was counted as completed if nebulization was marked as completed and there was no excess residual in the medication chamber. The medication chamber is the cup recorded on the investigational product administration case report form page.
EX	Count	EX_F01	Note:	Full dose refers to completion of all nebulizers as planned; partial dose refers to incomplete nebulization. Full and partial dose are independent of the presence or absence of excess residual in the medication chamber.
AE	Study day	AE_L01	Note:	Start day and end day of AEs were defined relative to the date of first dose of study drug.
AE	Derivation	AE_L02	Note:	AE Duration (days) was calculated as AE end date – AE start date + 1. Imputed AE start dates and imputed AE end dates were used in the case of partially missing dates. Any duration calculation that required use of imputed AE start date or imputed AE end date were identified by '*'.
AE	Dictionary	AE_L03	Note:	System Organ Class and Preferred Term are based on the Version 23.1 of the MedDRA coding dictionary.
AE	Definition	AE_L04	Note:	All adverse events that occurred within the 24 hours after completion of nebulization for subjects that had an adverse event of pyrexia within the 24 hours after completion of nebulization are listed.
AE	Definition	AE_L06	[1]	'N/A (During)' indicates that the adverse event occurred during nebulization.
AE	Definition	AE_L08	[1]	All adverse events that met the criteria for a febrile reaction or hypersensitivity reaction that occurred within the 24 hours after completion of

Data Type	Footnote Type	Code	Prefix	Footnote
				nebulization for subjects that had a febrile reaction or hypersensitivity reaction within the 24 hours after completion of nebulization are listed.
LB, CS	Abbreviation	CS_01		CS = clinically significant; NCS = not clinically significant
LB	Definition	LB_01	Note	The classification of Low, Normal, or High was based on the global laboratory reference ranges used across all sites. Clinical significance was assessed for out of range values based on the local laboratory reference ranges. Reference ranges provided were global laboratory reference ranges used across all sites.
QS	Abbreviation	QS_F01		CFQ-R = Cystic fibrosis questionnaire-revised
PE	Schedule	PE_L01	Note:	Either a comprehensive physical examination or a limited physical examination was performed. The limited physical examination included a review of respiratory and cardiovascular body systems at a minimum.
RE	Abbreviation	RE_L01	[1]	FEF2575 = FORCED EXPIRATORY FLOW 25-75% (L); FET = FORCED EXPIRATORY TIME (s); FEV1 = FORCED EXPIRATORY VOLUME IN 1 SECOND (L); FEV1FVC = FEV1/FVC (%); FEV1PP = PERCENT PREDICTED FEV1 (%); FVC = FORCED VITAL CAPACITY (L); FVCPP = PERCENT PREDICTED FVC (%); PEF = PEAK EXPIRATORY FLOW (L); TPEF = TIME TO PEAK EXPIRATORY FLOW (m); VEXT = EXTRAPOLATED VOLUME (m); VEXT/FVC = RATIO OF FEV1 TO FVC (%).
RE	Derivation	RE_L02	Note:	The baseline value was defined as the average of the results from testing on Day -1 and at pre-dose on Day 1.
RE	Derivation	RE_L03	Note:	The reference result was the predicted normal result based on age, gender, and height at screening.
CM	Dictionary	CM_L01	Note:	Anatomic Class, Therapeutic Class, and Preferred Name were based on the WHO Drug Global (2020-SEP) coding dictionary.
CM	Definition	CM_L02	Note:	Concomitant medications included all medications in use at date of first study drug dose or started after date of first study drug dose, any medications that started prior to the day of first dose of study drug with missing stop date or that were classified as ongoing. Prior medications included all medications that stopped prior to the day of first dose of the study drug or medications that started prior to the day of first dose of study drug with missing stop date. Medications with missing start and stop dates were classified as both prior and concomitant.

Translate Bio, Inc.
PROTOCOL NUMBER MRT5005-101

A Phase 1/2, Randomized, Double-Blind, Placebo-Controlled, Combined Single and Multiple Ascending Dose Study Evaluating the Safety, Tolerability, and Biological Activity of MRT5005 ([redacted] mRNA/[redacted] LNP) Administered by Nebulization to Adult [redacted] with [redacted] ic Fibrosis

Figure Specifications

VERSION DATE: 26 October 2021

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Figure Specifications

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General Programming Notes

The following instructions apply to all figure displays.

DISPLAY OUTPUTS FOR EACH PART
Each figure will be produced for each study part (A, B, D) unless otherwise specified. Figures will not be produced for the study overall. Each version of the figure will include the relevant study part in the header and in the figure identifier. For example, LB_FAA_F_X will be identified as LB_FAA_F_A for Part A and will include a header to show 'Part A'. A, B or D will be added to each display number.

PROGRAMMER NOTES

Programmer notes appear at the bottom of each figure display shell where applicable.

Dose groups for each part are as follow:

- Part A: MRT5005 8mg, MRT5005 16mg, MRT5005 20mg, MRT5005 24mg, Pooled Placebo
- Part B: MRT5005 8mg, MRT5005 12mg, MRT5005 16mg, MRT5005 20mg, Pooled Placebo
- Part D: MRT5005 4mg, Placebo

PAGE FORMATTING

The specifications for the format of each page are page size=47, line size=134, font=Courier, font size=8, and margin = 1.5" top, 1" bottom, left, and right.

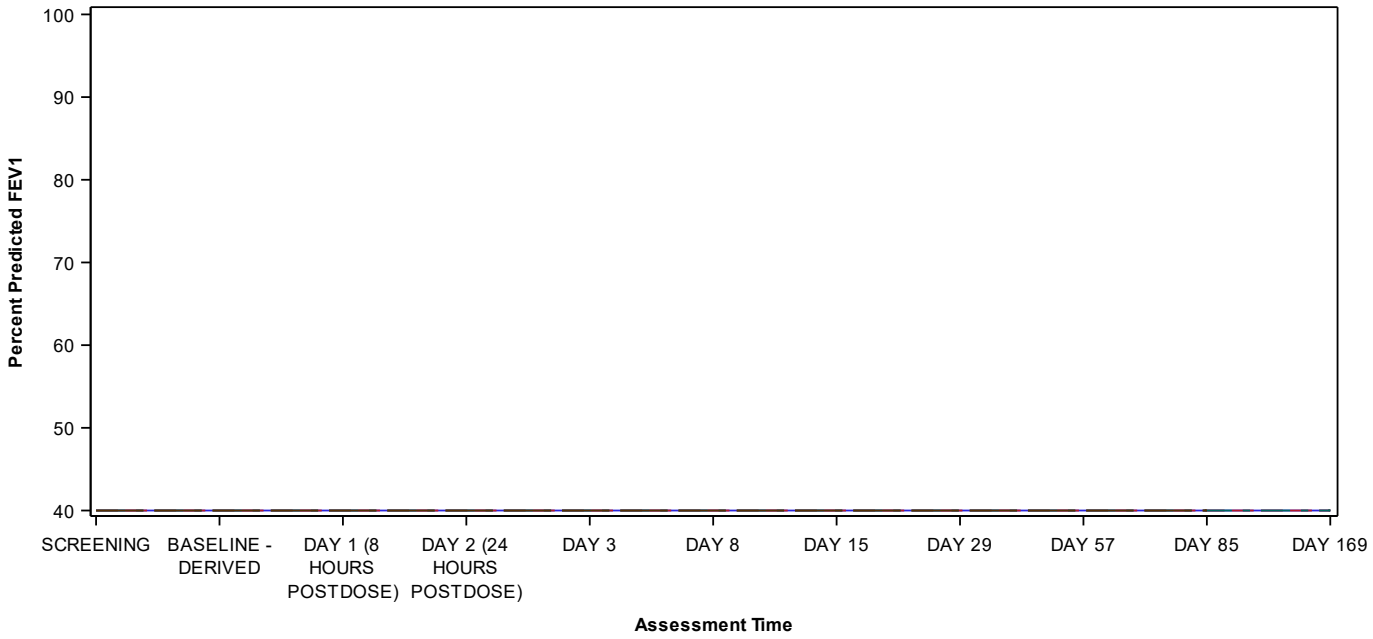
"Table Source: <Table Number>" will be printed on the right side of the footer for each figure.

PRECISION

No preliminary rounding should be performed; rounding should only occur after analysis. To round, consider digit to right of last significant digit: if < 5 then round down, if ≥ 5 then round up. Means, medians, 25th percentiles, 75th percentiles, and confidence intervals will be presented with one more decimal place than the precision of the data. Standard deviations will be presented with two more decimal places than the precision of the data. Percentages will be presented with one decimal place. Minimums and maximums will be presented with the same precision as the original data, with a maximum of 4 decimal places.

Figure 14.3.9.1.2 (RE_FAH_F_X)
Percent Predicted FEV1 Values by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Part: x
Dose Group: xxx



Note: RE_F01

X-axis: Assessment Time
Y-axis: Percent Predicted FEV1

Table Source: RE_TAA_F_X

Notes:

1) **Line plot of individual subject percent predicted FEV1 values over time**
2) **Separate page/plot for each part and dose group (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)**
3) **Include screening, baseline and all post-baseline visits**
4) **Include a legend to show subject ID (The placebo subject will be labeled in the legend)**
5) **Y-axis will range from 40%-110%**

6) For RE_FAH_F_D, replace footnote RE_F01 with RE_F01D

Non-unique figures for RE_FAH_F_X:

Figure 14.3.9.2.2 (RE_FAI_F_A)
Percent Predicted FEV1 Values to Day 29 by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: RE_TAA_F_A

Notes:
1) Repeat RE_FAH with the x-axis subset on visits on or before Day 29 for each Part A dose group: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo.
2) Time will be represented proportionally on the x-axis

Figure 14.3.9.2.2 (RE_FAI_F_B)
Percent Predicted FEV1 Values to Day 57 by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: RE_TAA_F_B

Notes:
1) Repeat RE_FAH with the x-axis subset on visits on or before Day 57 for each Part B dose group: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo.
2) Annotate x-axis to indicate the 5 dosing days using a symbol

Figure 14.3.9.2.2 (RE_FAI_F_D)
Percent Predicted FEV1 Values to Day 32 by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: RE_TAA_F_D

Notes:
1) Repeat RE_FAH with the x-axis subset on visits on or before Day 32 for each Part D dose group: 4 mg, Placebo.
2) Time will be represented proportionally on the x-axis
3) Replace footnote RE_F01 with RE_F01D
4) Time will be represented proportionally on the x-axis.

Figure 14.3.9.3 (RE_FAC_F_X)
Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAA_F_X

Notes:

1) **Repeat RE_FAH for the mean values (including standard error bars) for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo).**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **For RE_FAC_F_D, replace footnote RE_F01 with RE_F01D**

Figure 14.3.9.3.1 (RE_FAS_F_A)
Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 29
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAA_F_A

Notes:
1) **Repeat RE_FAH for the mean values (including standard error bars) with the x-axis subset on visits on or before Day 29 for each Part A dose group: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo.**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Time will be represented proportionally on the x-axis**

Figure 14.3.9.3.1 (RE_FAS_F_B)
Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 57
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAA_F_B

Notes:
1) **Repeat RE_FAH for the mean values (including standard error bars) with the x-axis subset on visits on or before Day 57 for each Part B dose group: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo.**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**

Figure 14.3.9.3.1 (RE_FAS_F_D)
Mean and Standard Error of Percent Predicted FEV1 Values by Dose Group and Visit Through Day 32
Population: Safety Analysis Set

Note: RE_F01D

Table Source: RE_TAA_F_D

Notes:
1) **Repeat RE_FAH for the mean values (including standard error bars) with the x-axis subset on visits on or before Day 32 for each dose group: (Part D: 4 mg and Placebo).**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Time will be represented proportionally on the x-axis**

Figure 14.3.9.4 (RE_FAL_F_X)
Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAA_F_X

X-axis: Assessment Time
Y-axis: Absolute Change from Baseline in ppFEV1

Notes:

1) **Repeat RE_FAH for mean absolute change from baseline values (including standard error bars) for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1**
4) **Time will be represented proportionally on the x-axis for RE_FAL_F_A and RE_FAL_F_D**
5) **For RE_FAH_F_D, replace footnote RE_F01 with RE_F01D**

Figure 14.3.9.4.1 (RE_FAM_F_A)
Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 29
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAA_F_A

X-axis: Assessment Time
Y-axis: Absolute Change from Baseline in ppFEV1

Notes:

1) **Repeat RE_FAH for mean absolute change from baseline values (including standard error bars) for each dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, and Pooled Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1 up to Day 29**
4) **Time will be represented proportionally on the x-axis**

Figure 14.3.9.4.1 (RE_FAM_F_B)
Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 57
Population: Safety Analysis Set

Note: RE_F01
Table Source: RE_TAA_F_B

X-axis: Assessment Time
Y-axis: Absolute Change from Baseline in ppFEV1

Notes:

1) **Repeat RE_FAH for mean absolute change from baseline values (including standard error bars) for each dose group: (Part: 8 mg, 12 mg, 16 mg, 20 mg and Pooled Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1 up to Day 57**

Figure 14.3.9.4.1 (RE_FAM_F_D)
Mean and Standard Error of Absolute Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 32
Population: Safety Analysis Set

Note: RE_F01D

Table Source: RE_TAA_F_D

X-axis: Assessment Time
Y-axis: Absolute Change from Baseline in ppFEV1

Notes:

1) **Repeat RE_FAH for mean absolute change from baseline values (including standard error bars) for each dose group: (Part D: 4 mg and Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1 up to Day 32**
4) **Time will be represented proportionally on the x-axis**

Figure 14.3.9.4.2 (RE_FAN_F_X)
Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAB_F_X

X-axis: Assessment Time
Y-axis: Relative Change from Baseline in ppFEV1 (%)

Notes:

1) **Repeat RE_FAH for mean relative change from baseline values (including standard error bars) for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1.**
4) **Time will be represented proportionally on the x-axis for RE_FAN_F_A and RE_FAN_F_D.**
5) **For RE_FAN_F_D, replace footnote RE_F01 with RE_F01D**

Figure 14.3.9.4.3 (RE_FAP_F_A)
Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 29
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAB_F_A

X-axis: Assessment Time
Y-axis: Relative Change from Baseline in ppFEV1 (%)

Notes:

1) **Repeat RE_FAH for mean relative change from baseline values (including standard error bars) for each dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, and Pooled Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1 up to Day 29.**
4) **Time will be represented proportionally on the x-axis**

Figure 14.3.9.4.3 (RE_FAP_F_B)
Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 57
Population: Safety Analysis Set

Note: RE_F01

Table Source: RE_TAB_F_B

X-axis: Assessment Time
Y-axis: Relative Change from Baseline in ppFEV1 (%)

Notes:

1) **Repeat RE_FAH for mean relative change from baseline values (including standard error bars) for each dose group: (Part B: 8 mg, 12 mg, 16 mg, 20 mg and Pooled Placebo)**
2) **Plot is only created for Part B**
3) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
4) **Include all visits after the pre-dose measure on Day 1 up to Day 57.**

Figure 14.3.9.4.3 (RE_FAP_F_D)
Mean and Standard Error of Relative Change from Baseline in Percent Predicted FEV1 Values by Dose Group and Visit to Day 32
Population: Safety Analysis Set

Note: RE_F01D

Table Source: RE_TAB_F_D

X-axis: Assessment Time
Y-axis: Relative Change from Baseline in ppFEV1 (%)

Notes:

1) **Repeat RE_FAH for mean relative change from baseline values (including standard error bars) for each dose group: (Part D: 4 mg and Placebo)**
2) **Note that all values will display on the same plot and the 'Dose Group' header will be removed**
3) **Include all visits after the pre-dose measure on Day 1 to Day 32.**
4) **Time will be represented proportionally on the x-axis**

Figure 14.3.4.1.1 (LB_FAA_F_X)
C Reactive Protein (mg/L) by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: LB_TAA_F_X

X-axis: Assessment Time
Y-axis: C Reactive Protein (mg/L)

Notes:
1) **Line plot of individual subject CRP values over time**
2) **Separate page/plot for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)**
3) **Include screening, baseline and all post-baseline visits**
4) **Y-axis minimum value will be zero, maximum will be 90**
5) **Time will be represented proportionally on the x-axis**

Figure 14.3.4.1.1.1 (LB_FAJ_F_A)
C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 29
Population: Safety Analysis Set

Table Source: LB_TAA_F_A

X-axis: Assessment Time
Y-axis: C Reactive Protein (mg/L)

Notes:
1) **Line plot of individual subject CRP values over time**
2) **Separate page/plot for each dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo)**
3) **Include screening, baseline and all post-baseline visits through Day 29**
4) **Y-axis minimum value will be zero, maximum will be 90**
5) **Time will be represented proportionally on the x-axis**

Figure 14.3.4.1.1.1 (LB_FAJ_F_B)
C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 57
Population: Safety Analysis Set

Table Source: LB_TAA_F_B

X-axis: Assessment Time
Y-axis: C Reactive Protein (mg/L)

Notes:
1) **Line plot of individual subject CRP values over time**
2) **Separate page/plot for each dose group: (Part B: 8 mg, 12 mg, 16 mg, 20 mg and Pooled Placebo)**
3) **Include screening, baseline and all post-baseline visits through Day 57**

4) Y-axis minimum value will be zero, maximum will be 90
5) Time will be represented proportionally on the x-axis

Figure 14.3.4.1.1.1 (LB_FAJ_F_D)
C Reactive Protein (mg/L) by Dose Group, Subject, and Visit Through Day 32
Population: Safety Analysis Set

Table Source: LB_TAA_F_D

X-axis: Assessment Time
Y-axis: C Reactive Protein (mg/L)

Notes:
1) Line plot of individual subject CRP values over time
2) Separate page/plot for each dose group: (Part D: 4 mg and Placebo)
3) Include screening, baseline and all post-baseline visits through Day 32
4) Y-axis minimum value will be zero, maximum will be 90
5) Time will be represented proportionally on the x-axis

Figure 14.3.4.2.1 (LB_FAB_F_X)
White Blood Cells (x10^9/L) by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: LB_TAB_F_X

X-axis: Assessment Time
Y-axis: White Blood Cells (x10^9/L)

Notes:
1) Line plot of individual subject WBC values over time
2) Separate page/plot for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)
3) Include screening, baseline and all post-baseline visits
4) Y-axis range will be 3 to 19
5) Time will be represented proportionally on the x-axis

Figure 14.3.4.3.1 (LB_FAC_F_X)
Neutrophils/Leukocytes (%) by Dose Group, Subject, and Visit
Population: Safety Analysis Set

Table Source: LB_TAB_F_X

X-axis: Assessment Time
Y-axis: Neutrophils/Leukocytes (%)

Notes:

1) **Line plot of individual subject neutrophil values over time**
2) **Separate page/plot for each part and dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, Pooled Placebo; Part B: 8 mg, 12 mg, 16 mg, 20 mg, Pooled Placebo; Part D: 4 mg, Placebo)**
3) **Include screening, baseline and all post-baseline visits**
4) **Y-axis range will be 5% - 90%**
5) **Time will be represented proportionally on the x-axis**

Figure 14.3.5.1.1 (VS_FAA_F_A)
Body Temperature Values by Dose Group, Subject, and Visit Through Day 7
Population: Safety Analysis Set

Table Source: VS_TAA_F_A

X-axis: Assessment Time
Y-axis: Temperature (C)

Notes:

1) **Line plot of individual subject temperature values over time**
2) **Separate page/plot for each dose group: (Part A: 8 mg, 16 mg, 20 mg, 24 mg, and Pooled Placebo)**
3) **Include baseline and only visits through Day 7 for Part A.**
4) **Y-axis range will be 35(C) - 40(C)**

Figure 14.3.5.1.1 (VS_FAA_F_B)
Body Temperature Values by Dose Group, Subject, and Visit Through Day 36
Population: Safety Analysis Set

Table Source: VS_TAA_F_B

X-axis: Assessment Time
Y-axis: Temperature (C)

Notes:

1) **Line plot of individual subject temperature values over time**
2) **Separate page/plot for each dose group: (Part B: 8 mg, 12 mg, 16 mg, 20 mg and Pooled Placebo)**
3) **Include baseline and only visits through Day 36 for Part B.**
4) **Y-axis range will be 35(C) - 40(C)**

Figure 14.3.5.1.1 (VS_FAA_F_D)
Body Temperature Values by Dose Group, Subject, and Visit Through Day 11
Population: Safety Analysis Set

Table Source: VS_TAA_F_D

X-axis: Assessment Time
Y-axis: Temperature (C)

Notes:

1) **Line plot of individual subject temperature values over time**
2) **Separate page/plot for each dose group: (Part D: 4 mg and Placebo)**
3) **Include baseline and only visits through Day 11 for Part D.**
4) **Y-axis range will be 35(C) - 40(C)**

Footnotes

Data Type	Footnote Type	Code	Prefix	Footnote
RE	Baseline	RE_F01	Note:	The baseline value was defined as the average of the results from testing on Day -1 and at pre-dose on Day 1.
RE	Baseline	RE_F01D	[1]	The baseline value was defined as the result from testing pre-dose on Day 1.

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[redacted]		Sent: 10/26/2021 12:37:12 PM Viewed: 10/26/2021 2:15:25 PM Signed: 10/26/2021 2:16:16 PM
Security Level: Email, Account Authentication (Required)	Signature Adoption: Pre-selected Style Signature ID: 2302C1A3-4255-4335-B26A-9E3BCC08FC15 Using IP Address: 108.49.127.187 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	
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Security Level: Email, Account Authentication (Required)	Signature Adoption: Pre-selected Style Signature ID: ECE62283-4997-4BFA-AB04-AFB2B0B4805A Using IP Address: 24.62.27.123 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	
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Rho, Inc. Security Level: Email, Account Authentication (Required)	Signature Adoption: Pre-selected Style Signature ID: E8BC91C1-B54B-4472-9F4A-53C7CA804C98 Using IP Address: 4.34.23.236 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	
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Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	10/26/2021 12:37:12 PM
Certified Delivered	Security Checked	10/26/2021 12:37:34 PM
Signing Complete	Security Checked	10/26/2021 12:38:06 PM
Completed	Security Checked	10/26/2021 4:02:34 PM

Payment Events	Status	Timestamps

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