STATISTICAL ANALYSIS PLAN
ALX0171-C203

A randomized, double-blind, multicenter, multiple-dose study of ALX-0171 versus placebo along with standard of care in Japanese infants and young children hospitalized for respiratory syncytial virus lower respiratory tract infection

Version: Final V 1.0

Date: 28 Nov 2018

Protocol:

CTP reference ALX0171-C203_13 Nov 2017

REVISION HISTORY

Version	Version Date	Author	Summary of Changes Made
Draft 0.1	12 Nov 2018	[redacted]	New documnent
Draft 0.2	15 Nov 2018	[redacted]	Updated addressing comments from team in Ablynx
Final 1.0	28 Nov 2018	[redacted]	Updated with comments from Ablynx and [redacted]

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LIST OF ABBREVIATIONS

AE	Adverse Event
BMI	Body Mass Index
CM	Centimeters
CS	Clinically Significant
CSR	Clinical Study Report
CSP	Clinical Study Protocol
cPAP	Continuous positive airway pressure
FU	Follow-Up
HFOT	High-flow oxygen therapy
ICU	Intensive Care Unit
IMP	Investigational Medicinal Product
IWRS/IVRS	Interactive web/voice response system
SAP	Statistical Analysis Plan
LRTI	Lower respiratory tract infection
NCS	Not Clinically Significant
PK	Pharmacokinetics
PT	Preferred Term
RSV	Respiratory Syncytial Virus
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
SpO2	Peripheral capillary oxygen saturation
TEAE	Treatment-emergent Adverse Event
TLF	Tables, Listings and Figures

1 INTRODUCTION

Study ALX0171-C203 is a randomized, double-blind, multicenter, multiple-dose study of ALX-0171 versus placebo along with standard of care in Japanese infants and young children aged 28 days to < 2 years hospitalized for RSV LRTI.

The purpose of statistical analysis plan (SAP) is to ensure that all the outputs which will be produced, and the statistical methodologies that will be used, are complete and appropriate to allow valid conclusions regarding the study objectives.
The analyses described are based on the final CSP Version 3.0 Section 5, dated, 13/Nov/2017. However, due to the halt of ALX0171 development in infants based on the results from the RESPIRE trial, this study was terminated early and an abbreviated CSR is planned instead of a Full CSR..
At the time of early termination, a total of 17 subjects were screened. 16 subjects were screened for cohort 1 out of whom 15 were enrolled and randomized; An IDMC meeting was held upon completion of this cohort. For cohort 2, 1 subject was screened but not randomized..
This SAP describes those analyses that will be performed for the abbreviated CSR.

2 STUDY OBJECTIVES

The objectives of this study were:

- To evaluate the safety, tolerability, and systemic pharmacokinetics (PK) of different doses of inhaled ALX-0171 in Japanese infants and young children hospitalized for respiratory syncytial virus (RSV) lower respiratory tract infection (LRTI).
- To evaluate the antiviral effect, clinical activity, immunogenicity and pharmacodynamics (PD) of different doses of inhaled ALX-0171 in Japanese infants and young children hospitalized for RSV LRTI.
  However, due to early termination, not all reported objectives as per protocol will be evaluated. Please refer to Section 9 for more details in change in statistical analysis plan from what is described in the protocol due to early termination.

3 STUDY DESIGN

3.1 Overall study design

Study ALX0171-C203 is a randomized, double-blind, multicenter, multiple-dose study of ALX-0171 versus placebo along with standard of care in Japanese infants and young children aged 28 days to < 2 years hospitalized for RSV LRTI. A schematic of the study design is presented in Figure 1.

The overall study duration was expected to be approximately 12 months, with the planned study duration for each subject approximately 28 days.

The following dose levels were planned to be evaluated in four consecutive cohorts:

- Dose 1: target dose of 1.5 mg/kg
- Dose 2: target dose of 3.0 mg/kg
- Dose 3: target dose of 6.0 mg/kg

- Dose 4: target dose of 9.0 mg/kg

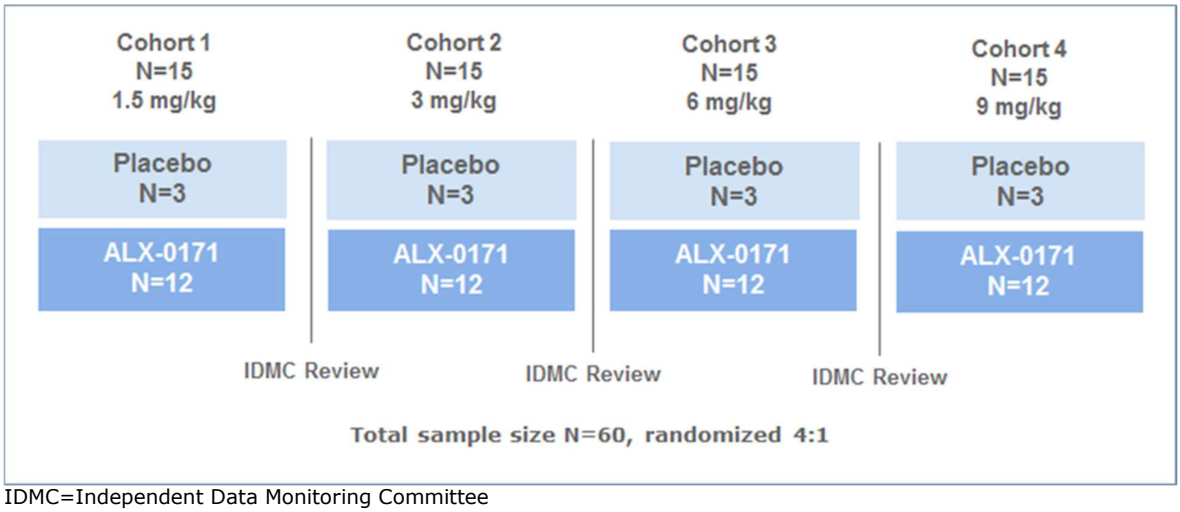
Each cohort was planned to consist of 15 subjects enrolled and randomly assigned to receive ALX-0171 or placebo, in an allocation ratio of 4:1 (N=12 active versus N=3 placebo per cohort). Study drug was planned to be administered once daily for 3 consecutive days and given along with standard of care treatment, which was determined by the Investigator according to institutional practice (taking into account the prohibited medications listed in CSP section 3.3.7.2).

In addition to the individual discontinuation criteria (see CSP section 3.4.2), criteria for stopping or pausing recruitment in each cohort and criteria to stop dose escalation were applied (see CSP section 3.1.1).

However, due to early termination of the trial, no subjects are screened for cohort 3 and cohort 4. Only 1 subject was screened for the second cohort but that subject was a screen failure. Enrollement was complete in Cohort 1 for which 16 subjects were screened and 15 of them were randomized into the treatment group ALX0171 1.5 mg/kg and placebo.

Therefore, the treatment groups ALX0171 3.0 mg/kg , ALX0171 6 mg/kg and ALX0171 9 mg/kg will contain no data and hence should not be reported in the respective outputs.

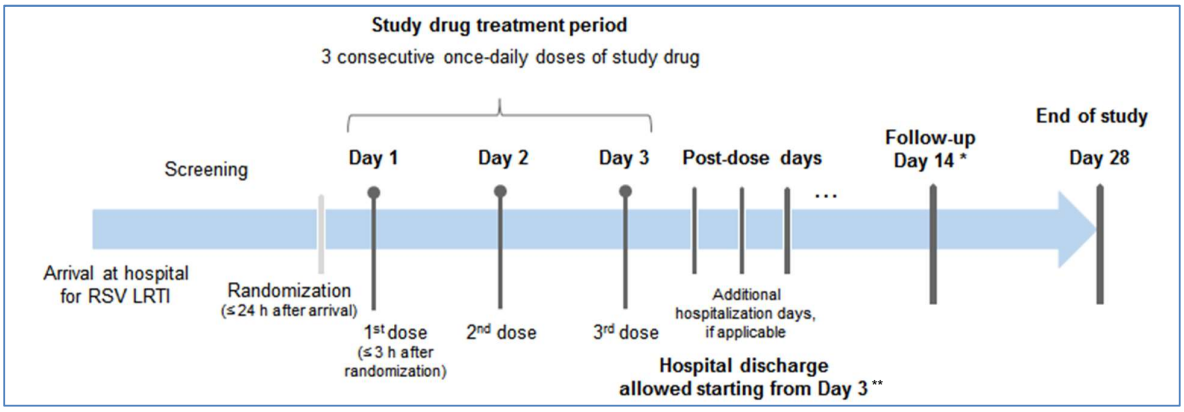
Figure 1: ALX0171-C203 – Study Design



IDMC=Independent Data Monitoring Committee

An overview of the study flow is shown in Figure 2.

Figure 2: ALX0171-C203 - Study Flow



*Or withdrawal visit at earlier time point in case of withdrawal
**Hospital discharge is allowed from Day 3 once all post-dose assessments have been completed.

3.2 Sample size

The planned sample size of 60 randomized and treated subjects was selected to provide information on the safety and tolerability of the different doses of ALX-0171 in Japanese infants and young children hospitalized for RSV LRTI. The sample size also allows for sufficient precision on the model estimated PK parameters, as described by Wang et al. [1] and it is expected to be informative on antiviral and clinical activity of ALX-0171.

However, due to early termination of the study, the enrollment could not be completed as planned. At the time of early termination, 17 subjects were screened and 15 randomized. All the analyses mentioned in the later sections of this document will be performed using data from these subjects.

3.3 Outcome measures to be considered for the abbreviated CSR

3.3.1 Safety Outcome Measures

- Treatment-emergent adverse events (TEAEs), as noted by healthcare staff and/or reported by parents/caregivers.
- Heart rate, respiratory rate (measured over a 1-minute interval) and SpO2
- Body temperature and body weight
- Physical examination includingthe skin, ears/nose/throat, heart auscultation, lung auscultation, and abdomen
- Safety lab assessments: planned two times during the study (at screening and at the follow-up (FU) visit) and will be performed by the local laboratory in order to allow timely availability of the results. The following clinical laboratory test results will be evaluated:
    - Clinical chemistry: alanine aminotransferase, aspartate aminotransferase, creatinine, sodium, potassium, chloride, C-reactive protein, γ-glutamyl-transferase, blood urea nitrogen
    - Hematology: hemoglobin, hematocrit, red blood cell count and indices, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count (or estimate), white blood cell count including differential (lymphocytes, neutrophils, monocytes, basophils, eosinophils).

3.3.2 Clinical Activity Outcome Measures

- Heart rate, respiratory rate (measured over a 1-minute interval) and SpO2
- Wheezing as assessed during lung auscultation
- Cough during the night and during the day
- Respiratory muscle retractions (supraclavicular, intercostal, and subcostal).
- Body temperature and body weight
- Occurrence of apnea episodes.

3.3.3 Medical Interventions Outcome Measures

- Length of hospital stay for RSV infection
- Level, method, and duration of supplemental oxygen therapy
- Initiation of invasive or non-invasive ventilation (e.g., continuous positive airway pressure [cPAP] or HFOT)
- Level, method and duration of invasive or non-invasive ventilation
- Transfer to ICU and duration of stay in ICU.

3.3.4 Virology Outcome Measures

- Viral load, assessed in samples obtained via nasal swabs and quantified using plaque cultures (to evaluate replication-competent virus) and by RT-qPCR (to evaluate viral mRNA).

3.3.5 Pharmacokinetic Outcome Measures

- Systemic (serum) concentrations of ALX-0171 will be used as a surrogate for local (lung) concentrations.

3.3.6 Immunogenicity Outcome Measures

- Immunogenicity will be assessed by evaluation of anti-drug antibodies (ADA) in serum. Confirmed positive ADA samples will also be evaluated for their neutralizing potential.

4 GENERAL ASPECTS FOR STATISTICAL ANALYSIS

4.1 Analysis populations

The following populations will be considered for the analyses required for the abbreviated CSR:

- **All Screened Subjects Population**: All subjects with an informed consent form signed from the parent(s)/legal guardian(s) or legally acceptable representative(s), who were screened for eligibility.
- **Safety Population**: All subjects who received at least 1 administration of study drug, as treated (i.e., using the treatment that the subject actually received).

4.2 General Methods

All original and derived parameters as well as population characteristics will be listed and described using summary statistics. Frequency counts (number of subjects [n] and percentages) will be made for each qualitative variable. Descriptive statistics (n, mean, standard deviation [SD], median, minimum and maximum) will be calculated for each quantitative variable, and will only be presented if n ≥ 2. If n=1, then only n and the mean will be displayed.

Repeated and unscheduled measurements will not be used for statistical analysis or summary tables, unless the repeated measurement was performed due to unreliable values/technical reasons, or the repeated measurement occurred prior to first study drug administration and is defined as the 'baseline'. The following rules will apply to any repeated measurements:

- If the repeated measurement occurs prior to the first study drug administration then the last obtained value of any repeated measurement will be used in the descriptive statistics.
- If the repeated measurement occurs after the first study drug administration then the original value of any repeated measurements will be used in the descriptive statistics.

All listings will include repeated and unscheduled measurements

All descriptive statistics will be presented by treatment group, and overall for disposition, demographic and baseline disease characteristics. The treatment groups were planned to be shown in the following order:

1. Placebo
2. Dose 1: target dose of 1.5 mg/kg

4.3 Baseline Definition

The Baseline value is defined as the value observed at the last timepoint before first study drug administration.

4.4 Rounding and decimal places

The following rules will be followed with regard to the number of decimal places and presentation of data in the tables and listings of safety data:

- All data will be listed according to the number of decimal places presented in the source data.
- Mean and median will be tabulated to one more decimal place than the source data.
- Minimum and maximum values will be tabulated to the same number of decimal places as the source data.
- Standard deviation (SD) will be tabulated to two more decimal places than the source data.
- A maximum of three decimal places will apply to all summary statistics.

4.5 Software and validation model

All statistical analyses will be performed using Statistical Analysis Software (SAS®) Version 9.3 or higher.

The following validation programming techniques, in agreement with PXL GDO EP SOPs, will be performed;

- Black box validation for ADaM datasets; double programming validation.
- White box validation for outputs; the reviewer has to execute the program step by step and to check and review the program as well as the datasets/log/output produced. The reviewer has also to verify the produced output and the data of the intermediate steps.

4.6 Statistical Significance Level

No formal statistical testing will be performed. All confidence intervals (CIs) will be calculated at a 95% level of confidence.

4.7 Missing Data

There will be no imputations of any missing data. All treated subjects will be included into the safety analyses as far as the data permit.

5 GENERAL CHARACTERISTICS

5.1 Subject Disposition

Subject disposition will be listed by subject and summarized (number and percentage of subjects) by treatment group and overall using all screened subjects. The tabulations will include the following information:

- Number of subjects randomized
- Number of subjects included in the safety population

Percentages will be based on the number of screened subjects.

In addition subject disposition will be summarized (number and percentage of subjects) by treatment group and overall using the safety population. The tabulations will include the following information:

- Number of subjects who completed the 3-day study treatment period
- Number of subjects who discontinued the study drug, with reasons for discontinuation
- Number of subjects who completed the trial
- Number of subjects who discontinued early from the trial, with reasons for termination

Percentages will be based on the number of subjects in the safety population.

Subject disposition by visit and by treatment group and overall will also be summarized (number and percentage of subjects) using the safety population.

5.2 Demographic and Baseline Characteristics

The following demographic and other baseline characteristics are recorded:

- Demographic characteristics:
  - Gestional ages (weeks)
  - Age (months)
  - Gender
  - Race
  - Asian specifications (if race is Asian)
  - Ethnicity
  - Body weight (kg) at baseline
  - Body weight (kg) categories at baseline;
    - 3.0 to < 4.0 kg
    - 4.0 to < 5.0 kg
    - 5.0 to < 7.0 kg
    - 7.0 to < 10.0 kg
    - 10.0 to < 12.0 kg
    - 12.0 to < 15.0 kg
  - Height (centimeters [cm])
  - Atopy history (yes/no/unknown)
  - Exposure to tobacco (yes/no)
  - Exposure to pets (yes/no)
  - Breastfed (yes/no)
- Baseline disease characteristics:
  - Heart rate (bpm)
  - Blood oxygen (SpO2) level (%)
  - Time since onset RSV signs and symptoms
  - RSV severity criteria:
    - Inadequate oral feeding (yes/no)
    - Inadequate oxygen saturation (yes/no)
    - Respiratory distress (yes/no)
    - Inadequate oral feeding (yes) and Inadequate oxygen saturation (yes) and Respiratory distress (yes)
    - Inadequate oral feeding (yes) and Inadequate oxygen saturation (yes)

Demographic and baseline characteristics will be listed by subject.

Demographic and baseline characteristics will also be summarized using descriptive statistics by treatment group and overall on the safety population.

5.3 Medical History

Medical history will be listed by subject, and will include at least the following: description of condition, body system, start date and end date (or ongoing, if applicable).

Medical history will also be summarized by treatment group and body system using the safety population.

5.4 Prior, Concomitant Medications and Oxygen Supplementation Therapies

Medications and/or oxygen supplementation therapies given on or after date of informed consent will be defined as concomitant medications. Medications and/or oxygen supplementation therapies that were given prior to date/time of informed consent, and which ended before date of informed consent will be classified as prior medications/ oxygen supplementation therapies.

If the start date is missing or unknown, the medication and/or oxygen supplementation therapy will be considered as concomitant (unless the end date is before the date/time of informed consent). If the end date is missing or unknown, the medication and/or oxygen supplementation therapy will be considered as concomitant.

When start and/or end dates of medications and/or oxygen supplementation therapies are only partially known, medications and/or oxygen supplementation therapies will be categorized using the following rules:

- If the partial end date is prior (<) to the date of informed consent (i.e., year or year & month is/are before the informed consent year or year & month) then the medication and/or oxygen supplementation therapy will be considered as prior.
- If the partial start date is equal or after (≥) the date of informed consent (ie, year or year & month is/are after or the same as the informed consent year or year & month) then the medication and/or oxygen supplementation therapy will be considered as concomitant.

Summary tables will be provided for prior medications/oxygen supplementation therapies, and for concomitant medications/oxygen supplementation therapies by treatment group, by presenting the number and percentage of subjects taking each medication, classified using World Health Organization (WHO) Drug Dictionary (March 2017 (Enhanced)), anatomical therapeutic chemical (ATC level 4 class) class and preferred term. Multiple records of the same preferred term for the same subject and the same ATC level 4 class will be counted only once. A listing by subject will also be produced for prior and concomitant medications.

5.5 Exposure to Study Medication and Treatment Compliance

Number of subjects receiving study medication will be summarized per nebulization and day by treatment group. Per each nebulization the following information will be summarized:

- Administration fully done (yes/no)
- Inhalation period interrupted (yes/no)
- Contact with face mask:

- Close contact with the face (and mouth and nose covered) most of the time (>75%)
- Close contact with the face (and mouth and nose covered) approx. half of the time (25%-75%)
- Close contact almost not achieved (<25% of the time)

- Problem occurrence during use of the device (yes/no)
- Device issue resulted in an adverse event (yes/no)

A listing by subject will also be produced.

6 SAFETY

Safety evaluation will take into account the recorded AEs, vital signs, laboratory assessments, physical examination findings, repiratory distress assessment, hospitalization and any other parameter that is relevant for safety assessment. All safety analyses will be based on the safety population.

6.1 Adverse Events

AEs will be coded by SOC and PT using the latest version of MedDRA available at the time of database lock. All adverse events recorded during the study will be listed with treatment emergent AEs flagged.

If an adverse event start date is missing or unknown, the adverse event will be considered as emergent (unless the adverse event end date is before the first dose of study drug).
When start and/or end dates of an adverse event are only partially known, adverse events will be categorized using the following rules:

- If the end time is missing and the end date is before (<) the first dose of study drug, then the adverse event will not be considered as emergent.
- If the partial end date is before (<) the first dose of study drug (i.e., year or year & month is/are before the first dose of study drug year or year & month), then the adverse event will not be considered as emergent.
- If the start time is missing and the start date is equal or after (≥) the first dose of study drug, then the adverse event will be considered as emergent.
- If the partial start date is equal or after (≥) the first dose of study drug (ie, year or year & month is/are after or the same as the first dose of study drug year or year & month), then the adverse event will be considered as emergent.

No imputation will be done of missing/partial date(time) fields. The dates and times will be presented in the listings as captured in the eCRF.

TEAEs or treatment-emergent SAEs are events temporally associated with the use of study drug (occurring during or after the first dose of study drug, or worsening in severity (for pre-existing conditions)), whether considered related to the study drug or not.

In the TEAE overview table, number and percentage of subjects for the following items will be provided:

- Subjects with at least one treatment-emergent adverse event (TEAE)
- Subjects with at least one serious TEAE
- Subjects with at least one TEAE leading to death
- Subjects with at least one severe TEAE as classified by the investigator
- Subjects with at least one TEAE for which the study drug was interrupted
- Subjects with at least one TEAE for which the study drug was discontinued
- Subjects with at least one TEAE that was considered treatment-related (relationship to study drug is related or possibly related or missing) by the investigator.
- Subjects with at least one serious TEAE that was considered treatment-related (relationship to study drug is related or possibly related or missing) by the investigator.

The incidence (number and percentage) of TEAEs will be summarized by SOC/PT, severity (mild, moderate, severe, missing) and relationship to study drug (related, possibly related, unlikely related, not related, not applicable, missing) for each treatment group.

Each AE listing will include;

- Subject number/ site
- Start and stop date/time of each nebulization
- AE description
- AE system organ class
- AE preferred term (flagging serious TEAEs with an asterisk *)
- TEAE indicator flag
- AE start and end date/time
- AE onset day
- AE duration
- AE seriousness
- AE severity
- AE drug relatedness
- AE relatedness to study procedure
- AE outcome
- AE action taken
- Concomitant therapy started (yes/no)

The following counting rules for TEAEs will be used:

A subject experiencing AEs with the same SOC or PT more than once after dosing will be counted as following;

- For tables counting TEAEs by intensity, only the most severe TEAE will be counted for each subject within the corresponding SOC/PT.
- For tables counting TEAEs by relationship, only the most related TEAE will be counted for each subject within the corresponding SOC/PT.

The denominator for the percentages will be the number of subjects in the safety population for each treatment group.

6.2 Adverse events leading to study drug discontinuation

TEAEs leading to discontinuation from the study drug will be listed for each subject and summarized by SOC/PT for each treatment group.

6.3 Serious adverse events

Serious TEAEs will be summarized by SOC/PT for each treatment group.

SAEs will be listed by subject.

6.4 Non-Serious adverse events

Non-Serious TEAEs will be summarized by SOC/PT for each treatment group.

6.5 Laboratory Evaluations

Blood sampling for laboratory clinical chemistry and hematology will be obtained at screening and at Follow Up and results will be presented in standard international (SI) units.

The following parameters will be measured:

- Hematology: hemoglobin, hematocrit, red blood cell count and indices, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count (or estimate), white blood cell count including differential (lymphocytes, neutrophils, monocytes, basophils, eosinophils).
- Clinical chemistry: alanine aminotransferase, aspartate aminotransferase, creatinine, sodium, potassium, chloride, C-reactive protein, γ-glutamyl-transferase, blood urea nitrogen.

A listing for results outside the reference ranges or clinical significance will be produced and will include the result, date and time of measurement, change from Baseline, reference range and flags for measurements that are outside the reference range (where applicable). Abnormal values will be flagged as "L" (for values lower than the lower limit of the reference range) and "H" (for values higher than the upper limit of the reference range). Clinical significance(abnormality) will be indicated as abnormal, "CS" (clinically significant) or abnormal, "NCS" (not clinically significant). The listing will present all laboratory data for subjects with an out-of-range or clinical significant result.

Summary tabulations (absolute and change from baseline values) of hematology and clinical chemistry laboratory tests will be presented by treatment group and time point.

Additional tabulations will present the shift in abnormality (L/N/H/L+H) at the worst post-baseline time point, including unscheduled measurements, versus the baseline abnormality (L/N/H). Only parameters with a given normal range will be presented.

Any safety laboratory values given as '<xx' or '>xx' in the database will be imputed with the absolute value of the number without the sign (e.g., <2.2 will be imputed as 2.2) for the calculation descriptive statistics. Orginal value ‘<xx’ where xx equals the lower limit of the normal range will be classified as abnormaly low. Orginal value ‘>xx’ where xx equals the

upper limit of the normal range will be classified as abnormaly high. In the listings, no imputations will be performed and all data will be displayed as recorded in the database.

6.6 Physical Examination

A physical examination including heart auscultation, examination of abdomen, skin, ears/nose/throat will be performed as described in the schedule of assessments as outlined in the CSP (section 3.6.3.6). For each body system, any abnormalities will be documented.

All reported abnormalities with the assessment of Clinical Significance in the physical examination will be listed by subject and time point for each body system.

6.7 Vital Signs and Respiratory Distress Assessment (RDA)

Summary tabulations (absolute values and changes from baseline (if applicable)) for vital signs (temperature (°C), weight (kg), heart rate (HR) (bpm), blood oxygen (Sp02) level (%), and respiratory rate (breaths/min)) will be presented by treatment group and time point. Measurements obtained at baseline and post-baseline will be included in the tabulations for the treatment received.

Hear Rate collection method, SpO2 measurement location, oxygen flow delivery (yes/no), duration of oxygen supplementation (hours) and RDA tests (lung auscultation (wheezing, lung fields affected by wheezing, crackles/crepitations), respiratory muscle retractions (supraclavicular, intercostal, subcostal), daytime coughing and night-time coughing) will be tablulated by treatment group and time point. Measurements obtained at baseline and post-baseline will be included in the tabulations for the treatment received.

6.8 Hospitalization, ICU, Apnea and Ventilation

Duration of hospitalization will be summarized by treatment group. Hospitalization events will be described using Kaplan- Meier method; the number of events (the hospital discharge), number of censored values (subjects who are not discharged from the hospital at the time of early termination), median and quartiles of time to event with 95%CI will be summarized by treatment group.

The duration of hospitalization is defined as the difference between admission and discharge and will be computed in days using the following formula:

- For subjects who were discharged:

  (Discharge date/time – admission date/time) / 86400

- For subjects who were still hospitalized or in ICU at the time of early termination, the censoring date will be the date of termination of the trial and the duration of hospitalization will be derived using the following formula

  Trial termination date – admission date + 1

Missing time will be defined as follows for the calculation of duration:

- If the admission time is missing then it is estimated as 00:01

- If the discharge time is missing then it is estimated as 16:00

Hospitalization and ICU duration days, as well as apnea epsiodes and ventilation will be listed by subject.

7 ANALYSIS OF PHARMACOKINETICS

Individual study drug concentrations, actual sampling time and actual sampling times relative to second study drug administration time will be listed by treatment group and subject.

The sampling time relative to the second study drug administration time will be computed in hours as follows:

- (Start date/time of sampling – start date/time of second study drug administration) / 3600

The sampling time will be negative for blood samples taken on Day 2 pre-dose.

8 IMMUNOGENICITY ANALYSIS

Immunogenicity will be assessed through listing of individual results by subject, as described in section 8.2.

8.1 Available data

8.1.1 Anti-Drug Antibodies ADA

Immunogenicity of ALX-0171 will be monitored in this trial using MSD-based homogeneous bridging ADA assay via a tiered approach. In a first step, samples are evaluated in a screening assay and are scored possibly ADA positive based on the screening cut-point (SCP), allowing a 5% false positivity rate. Positively screened samples are subsequently analyzed in a confirmation assay, which is a drug displacement assay to confirm the specificity of the ADA screening result. All positively confirmed samples are subsequently analyzed in an end-point titration assay to determine the antibody titer. The log10(titer) will be reported. The titer represents the last dilution factor of the sample's titration series still scoring positive in the ADA assay. Samples scoring negative in the ADA assay are not titrated and the respective log10(titer) is reported as <log10(Minimal required dilution [MRD]) with MRD=24, i.e. log10(titer)<1.38.

For each subject, immunogenicity results will be classified based on the presence of pre-existing antibodies (pre-Ab) and the presence of treatment-emergent (TE) ADA, as shown in Table 1. Classification will be performed by the Bioanalytical laboratory (Ablynx GLP-Pharma) performing the ADA sample analysis and reporting both log10(titer) and subject classification.

Table 1: Subject Classification Based on Pre-Ab and TE ADA Status (ADA Assay)

Subject classification
1. pre-Ab NEG – TE ADA NEG
2. pre-Ab NEG – TE ADA POS
3. pre-Ab POS – TE ADA NEG
4. pre-Ab POS – TE ADA POS

5. pre-Ab POS – TE ADA Equivocal
6. TE ADA inconclusive: pre-Ab NEG - post-dose missing
7. TE ADA inconclusive: pre-Ab POS - post-dose missing
8. TE ADA inconclusive: pre-dose missing - post-dose NEG
9. TE ADA inconclusive: pre-dose missing - post-dose POS

NEG: negative; POS: positive

Note: Subject classification 'Inconclusive TE ADA' (that is generally used in case drug tolerance is exceeded) is not included here since drug washout samples are available for ADA testing.

8.1.2 Neutralizing Anti-Drug Antibodies (NAb)

All samples confirmed positive in the ADA assay will be further characterized in the NAb assay. NAb assay results will be reported as values (ratio is optical density (OD) value over negative control (NC)). No titration will be performed.
Subjects will be classified based on their pre-dose status (i.e. baseline visit) and status on treatment as shown in Table 2. Subject classification based on NAb will be performed by the external provider (Eurofins, UK) performing NAb sample analysis and reporting both ratio (for all received samples) and NAb subject classification. Subjects with no positive ADA samples and no missing visits, will not be analyzed in the NAb assay and will be classified as pre-dose NEG – NEG on treatment.

Table 2: Subject Classification Based on Pre-Dose and TE NAb Status (NAb Assay)

Subject classification
1. pre-dose NEG – NEG on treatment
2. pre-dose NEG – POS on treatment
3. pre-dose POS – NEG on treatment
4. pre-dose POS – POS on treatment
5. pre-dose NEG – post-dose missing
6. pre-dose POS – post-dose missing
7. pre-dose missing - NEG on treatment
8. pre-dose missing – POS on treatment

NEG: negative; POS: positive

8.2 Immunogenicity Listing

Listing of individual results by treatment group, by subject for all immunogenicity parameters (ADA log10(titer) and NAb response ratio as well as ADA and NAb subject classifications) at each time point will be produced. Samples not evaluated in the NAb assay will be indicated as not analyzed (NA).

ADA (log10 titer) measured for specifics SAEs will be described in the listing presenting all SAEs by subject. "N/A" will be reported for SAEs where no ADA analysis was performed.

9 CHANGE FROM ANALYSIS PLANNED IN PROTOCOL

This section describes all changes from planned analyses in the protocol, after the protocol approval, but before the lock of the database, which did not lead to a protocol amendment.

1. Due to early termination of the trial , an abbreviated CSRwill be produced instead of a full CSR and only a subset of all the statistical analyses that were planned in the protocol will be performed. . Following analyses have been excluded:

    a. Evaluation of Antiviral effect: A listing showing the viral load data for Plaque assay and Rt-qPCR over time will be produced. Any other statistical analyses planned in the protocol, e.g. time-to-below the limit of quantification (BQL), time-to-undetectability, time-weighted average change from baseline up to Day 3 and Day 14, number and percent of subjects with undetectable RSV (from Day 1 to Day 14), number and percent of subjects with BQL and change from baseline in viral load, will not be performed
    b. Evaluation of clinical activity:
        i. No statistical analysis will be done on RDAI score, RACS and Global Severity Score (GSS)
        ii. No statistical analyses will be included in the CSR on Clinical response, Adequate feeding , adequate oxygen supply
    c. Correlation of immunogenicity: a listing of immunogenicity data (ADA and NAb) (as mentioned above in Section 8) will be produced. Statistical analysis for potential correlation between pre-Ab, TE ADA or NAb on safety, PK and efficacy, will not be performed. No descriptive summary statistics will be generated. There will also be no tabulation of prevalence of pre-Ab and incidence of ADA.
    d. Evaluation of PD: The PD characteristics will not be reported in the abbreviated CSR (as serum levels of KL-6 will not be measured) and therefore no outputs will be produced

    e. Parent(s)/Caregiver(s) assessment: No analysis will be done

10 CONVENTIONS

10.1 Visit Windows

For post-baseline assessments, the CRF visit label will be used for the summaries. No windowing will be done.
For the full Schedule of Events refer to CSP, Version 3.0 (Page 24)

10.2 Computation of Derived Data

The following calculations and derivations will be used:

- Change from baseline of parameter: (visit value of parameter – baseline value of parameter)
    - If either the baseline or post-baseline value is missing, the change from baseline is set to missing.
- Duration of AE (days) = (end date - start date +1)

  - If either the end or start date is incomplete or missing, the duration of AE is set to missing.
  - If AE ongoing at the end of the trial then AE duration = trial termination date – AE start date + 1. In the listing the duration will be presented as '>x days' rather than 'x days'.
- Hospitalization or ICU duration (days) = discharge date/time – admision date/time
  - If either the end or start time is missing, the duration is calculated using the date part only then; duration = discharge date – admission date +1.
  - If the subject is still hospitalized or in ICU at the end of the trial then the duration = trial termination date – admission date +1
- Time since onset RSV signs and symptoms (days) = date of ICF – start date of symptom + 1.
- AE onset day = AE start date - first study drug administration date + 1 (when AE start date ≥ first study drug administration date
  - If AE start date < first study drug administration date then; AE onset day = AE start date - first study drug administration date
- Duration of oxygen supplementation (hours) is defined as total time of reported oxygen supply according to oxygen supplementation form.
  - If the time is missing or the date is incomplete then the duration is set to missing.

10.3 SAS procedures

Hospitalization events will be described using Kaplan- Meier method. The following SAS code will be used;

```
PROC LIFETEST data=XXX;
   TIME Study Day * Status(0);
        [Where Status = 0 means not discharge event for the subject]
   STRATA Treatment Group;
RUN;
```

11 REFERENCE LIST

[1] Wang, Y., et al., Clarification on precision criteria to derive sample size when designing pediatric pharmacokinetic studies. Journal of clinical pharmacology, 2012. 52(10): p. 1601-6.

12 PROGRAMMING CONSIDERATIONS

12.1 General

The following details the requirements and specifications for the programming and presentation of the TLFs, as set out in the TLF shells.

- A separate RTF document will be created for each TLF.
- All TLFs will be produced in a landscape format, as far as is feasible.
- The margin, page size specifications are stipulated below and will used for the presentation of all TLFs:

Item:	Specification:
Page Layout	Landscape
Paper Size	A4 (21cm x 29.7cm)
Margins (Top, Bottom, Left and Right)	2.54 cm
Header	1.25 cm
Footer	1.25 cm

- The standard font size and font type are "8 point", "Courier New" for all TLFs.
- Every page of each output will have a header indicating the Sponsor name (i.e., Ablynx NV) and protocol number (i.e., ALX0171-C203) (to be presented as set out in the example below).
- Every page of each output will contain a footer indicating the program name and the date and time when the output was produced (to be presented as set out in the example below).
- Every page of each output will contain a page number written in the format "Page X of Y" (to be presented as set out in the example below).
- Numbering of TLFs will follow ICH E3 guidance
- The following treatment group labels will be used for all TLFs in the following order (any treatment group with no subjects will not be displayed):
  1. Placebo
  2. ALX-0171 1.5 mg

Dates and times will be listed using date format ' DDMMMYYYY ' and 24h clock format 'hh:mm', respectively.

All tables will be decimal aligned.

For all outputs containing calculated changes from baseline, the reference point will be specified in a footnote.

For all outputs containing calculated percentages, the denominator for the percentages will be specified in a footnote.

12.2 Headers

The Headers will contain Information for the Sponsor, Study Identifier and [redacted] Study No. An example is presented below:

Ablynx NV Page X of Y
ALX0171-C203/[redacted] 234611 Confidential

12.3 Display Titles

The display titles will include the category (Table/Listing), the number, the title and the analysis population.

12.4 Column Headers

Column headers and column contents will be equally aligned. Column headers will be aligned left for Parameters and Statistics. Results columns will be centered.

12.5 Body of Data Display

12.6 General Conventions

The following general conventions will be applied:

1. Always put percentages between ( ).
2. If percentage is zero, don't print the percentage.
3. How to report missing data (eg, in demography table):
    - Include missing category without percentage and calculate % based on the number of subjects with available data

Gender, n (%)	N=12
Male	6 (60.0)
Female	4 (40.0)
Missing	2

4. AE TLFs: always report the MedDRA version in a footnote
5. If there's no data to be included in the output (e.g., no SAEs), add a line with 'No data to present'.

12.7 Table Conventions

The following conventions will be applied for summary tables:

- Units will be displayed (where available)
- For categorical variables, the number of observations and percentages between brackets will be displayed.
- All the categories of a categorical variable will be displayed, even if the number of observation is zero for a given category.
- If the number of observation is zero, then the percentage will not be displayed.
- The denominator on which the percentages are based will be indicated in footnote.
- In case of missing data, a missing category without percentage will be displayed.
- If there are no data to be described in the output (e.g, no SAEs), a line "no data to present" will be displayed.

- Sorting of AE summary tables: by decreasing frequency in SOC and PT (overall). If more than one term with the same frequency, then sort those terms alphabetically.
- Sorting of prior/concomitant medication summaries: by decreasing frequency (overall)

13 INDEX OF TABLES

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Population: all screened population.

Table 14.1.1.2: Treatment and Trial termination: Tabulation
Population: safety population.

Table 14.1.1.3: Subject disposition by visit: Tabulation
Population: safety population.

Table 14.1.2.1: Demographic data: Tabulation and descriptive statistics
Population: safety population.

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Population: safety population.

Table 14.1.2.3: Medical History
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Population: safety population.

Table 14.1.2.5: Concomitant therapies by generic term
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Table 14.3.1.1: Treatment-emergent adverse events: Summary table
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Table 14.3.1.2: Treatment-emergent adverse events: Tabulation of all adverse events
Population: safety population.

Table 14.3.1.3: Treatment-emergent adverse events: Tabulation of all adverse events by severity
Population: safety population.

Table 14.3.1.4: Treatment-emergent adverse events: Tabulation of serious adverse events
Population: safety population.

Table 14.3.1.5: Treatment-emergent adverse events: Tabulation of all adverse events by relationship to study drug
Population: safety population.

Table 14.3.1.6: Treatment-emergent adverse events: Tabulation of the events for which the study drug was discontinued
Population: safety population.

Table 14.3.1.7: Treatment-emergent adverse events: Tabulation of all non-serious adverse events
Population: safety population.

13.3 Safety: Laboratory

Table 14.3.2.1: Laboratory data: Descriptive statistics of the actual values and changes from baseline per time point
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Table 14.3.2.2: Laboratory data: Cross-tabulation of the worst-case abnormalities
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13.4 Safety: Vital Signs

Table 14.3.3.1: Vital signs: Descriptive statistics of the actual values and changes from baseline per time point
Population: safety population.

Table 14.3.3.2: Vital signs: Tabulations per time point
Population: safety population.

13.5 Safety: Respiratory Distress Assessment

Table 14.3.4.1: RDA: Descriptive statistics of the actual values and changes from baseline in respiratory rate per time point
Population: safety population.

Table 14.3.4.2: RDA: Tabulations per time point
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13.6 Hospitalization

Table 14.3.5.1: Duration of hospitalization: tabulation
Population: safety population.

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14.2 Safety: Adverse Events

Listing 16.2.2.1: Adverse events
Population: safety population.

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Population: safety population.

Listing 16.2.2.3: Adverse events leading to study drug discontinuation
Population: safety population.

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14.3 Safety: Laboratory

Listing 16.2.3.1: Laboratory data: Abnormalities
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14.4 Safety: Hospitalization

Listing 16.2.4.1: Duration of Hospitalization
Population: safety population.

Listing 16.2.4.2: Duration of ICU
Population: safety population.

Listing 16.2.4.3: Apnea and ventilation
Population: safety population.

14.5 Safety: Physical examination

Listing 16.2.5.1: Physical examination: Abnormalities
Population: safety population.

14.6 Virology

Listing 16.2.6.1: Viral Load
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Listing 16.2.7.1: Study Drug Concentrations and Sampling Times
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14.8 Immunogenicity

Listing 16.2.8.1: Immunogenicity – Full Data
Population: Safety Population

15 MOCK TLFS

15.1 Mock Tables

Table 14.1.1.1: Subject Disposition: Tabulation (All Screened Subjects)

Disposition	Statistic	Placebo	ALX-0171 1.5 mg	Overall (N = XX)
All Screened Subjects	n (%)			XX (100.00)
Subjects Randomized	n (%)	XX	XX	XX (XX.XX)
Subjects included in the Safety population	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects screened; n: The number of subjects in the specific category;
%: for safety population, calculated using the number of randomized subjects as the denominator) for each treatment group; for randomized population, calculated using the number of screened subjects as the denominator

Table 14.1.1.2: Treatment and Trial Termination:Tabulation (Safety Population)

	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)	Overall (N = XX)
Subjects who Completed the 3-day Study Treatment Period	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Subjects Discontinued the Study Treatment Period	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Adverse Event	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Prohibited Medications	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Lost to Follow-up	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Non-Compliance with Study Drug	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Consent Withdrawn by Parent/Legal Guardian	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Death	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Study Terminated by sponsor	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Code Broken	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Physician's Decision	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Sponsor's Decision	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Other	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Subjects who Completed the Trial	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Subjects Discontinued the Trial	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Adverse Event	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Prohibited Medications	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Lost to Follow-up	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Non-Compliance with Study Drug	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Consent Withdrawn by Parent/Legal Guardian	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
------	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects in the safety population; n: The number of subjects in specific category; %: calculated using the number of subjects in the safety population as denominator (n/N*100)..

Table 14.1.1.3: Subject Disposition by Visit: Tabulation (Safety Population)

Visit	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)	Overall (N = XX)
Screening	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Day 1	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Day 2	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Day 3	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Post treatment visit 1	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

Follow-up or Withdrawal	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
End of study	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number in the safety population as the denominator (n/N*100).

Table 14.1.2.1: Demographic Data: Tabulation and descriptive statistics (Safety Population)

Characteristic	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)	Overall (N = XX)
Age (Months)		n	XX	XX	XX
		Mean	XX.X	XX.X	XX.X
		SD	XX.XX	XX.XX	XX.XX
		Median	XX.X	XX.X	XX.X
		Minimum	XX	XX	XX
		Maximum	XX	XX	XX
Gestational Age (Weeks)		n	XX	XX	XX
		Mean	XX.X	XX.X	XX.X
		SD	XX.XX	XX.XX	XX.XX
		Median	XX.X	XX.X	XX.X
		Minimum	XX	XX	XX
		Maximum	XX	XX	XX
Gender	Male	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Female	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Ethnic Origin	Not Allowed to Ask per Local Regulations	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Hispanic or Latino	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Not Hispanic or Latino	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Race	White	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Asian	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	--------	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
If Asian	Japanese	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Far East Oriental	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)

Table 14.1.2.1: Demographic Data: Tabulation and descriptive statistics (Safety Population)

Characteristic	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)	Overall (N = XX)
	Asiatic Indian	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
Height at Baseline (cm)		n	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX
		SD	XX.XXX	XX.XXX	XX.XXX
		Median	XX.XX	XX.XX	XX.XX
		Minimum	XX.X	XX.X	XX.X
		Maximum	XX.X	XX.X	XX.X
Weight at Baseline (kg)		n	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX
		SD	XX.XXX	XX.XXX	XX.XXX
		Median	XX.XX	XX.XX	XX.XX
		Minimum	XX.X	XX.X	XX.X
		Maximum	XX.X	XX.X	XX.X

SD: standard deviation.
N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects with non missing data in the safety population as the denominator (n/(N non missing)*100).

Note to Programmer: Please display the following variables;

- Weight Categories (kg)
- Atopy History (yes/no/unknown)
- Exposure to Tobacco (yes/no)
- Exposure to Pets (yes/no)
- Breastfed (yes/no)

Table 14.1.2.2: Baseline disease characteristic: Tabulation and descriptive statistics (Safety Population)

Characteristic	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)	Overall (N = XX)
Categorical Parameters	Category 1	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Category 2	n (%)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	...				
Continuous Parameters		n	XX	XX	XX
		Mean	XX.XX	XX.XX	XX.XX
		SD	XX.XXX	XX.XXX	XX.XXX
		Median	XX.XX	XX.XX	XX.XX
		Minimum	XX.X	XX.X	XX.X
		Maximum	XX.X	XX.X	XX.X

SD: standard deviation.
N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects with non missing data in the safety population as the denominator (n/(N non missing)*100).

Note to Programmer: Please display the following variables;

- Heart Rate (bpm) at baseline
- Blood Oxygen (SpO2) level (%) at baseline
- Time since onset RSV signs and symptoms (days)
- RSV Severity Criteria:
    - Inadequate Oral Feeding (yes/no)
    - Inadequate Oxygen Saturation (yes/no)
    - Respiratory Distress (yes/no)
    - Inadequate Oral Feeding (yes) and Inadequate Oxygen Saturation (yes) and Respiratory Distress (yes)
    - Inadequate Oral Feeding (yes) and Inadequate Oxygen Saturation (yes)

Table 14.1.2.3: Medical History (Safety Population)

Body System Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any medical history	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXXXXXXXX	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXXXXXXXX	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXXXXXXXX	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXXXXXXXX	n (%)	XX (XX.XX)	XX (XX.XX)
...			
...			

N: Number of subjects in the safety population; n: Number of subjects in the specific category; %: Calculated using the number of subjects in the safety population as the denominator (n/N*100).

Table 14.1.2.4: Prior therapies by generic term (Safety Population)

ATC Level 4 Class Generic Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any prior therapy	n (%)	XX (XX.XX)	XX (XX.XX)
ATC Level 4 Class	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 1	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 2	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 3	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 4	n (%)	XX (XX.XX)	XX (XX.XX)
...			
...			

N: Number of subjects in the safety population; n: Number of subjects in the specific category; %: Calculated using the number of subjects in the safety population as the denominator (n/N*100).
All Therapies are coded with WHO-DD Version March 2017 (Enhanced)

Table 14.1.2.5: Concomitant therapies by generic term (Safety Population)

ATC Level 4 Class Generic Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any concomitant therapy	n (%)	XX (XX.XX)	XX (XX.XX)
ATC Level 4	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 1	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 2	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 3	n (%)	XX (XX.XX)	XX (XX.XX)
Generic Term 4	n (%)	XX (XX.XX)	XX (XX.XX)
...			
...			

N: Number of subjects in the safety population; n: Number of subjects in the specific category; %: Calculated using the number of subjects in the safety population as the denominator (n/N*100).
All Therapies are coded with WHO-DD Version March 2017 (Enhanced)

Table 14.1.2.6: Exposure to study medication: Tabulation (Safety Population)

Day	Characteristic	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
XX	Nebulization 1		n (%$)	XX (XX.XX)	XX (XX.XX)
	Was the administration fully done?	Yes	n (%)	XX (XX.XX)	XX (XX.XX)
		No	n (%)	XX (XX.XX)	XX (XX.XX)
	Was the inhalation period interrupted?	Yes	n (%)	XX (XX.XX)	XX (XX.XX)
		No	n (%)	XX (XX.XX)	XX (XX.XX)
	Contact with face mask	Most	n (%)	XX (XX.XX)	XX (XX.XX)
		Half	n (%)	XX (XX.XX)	XX (XX.XX)
		Almost not	n (%)	XX (XX.XX)	XX (XX.XX)
	Problem occurrence during use of the device	Yes	n (%)	XX (XX.XX)	XX (XX.XX)
		No	n (%)	XX (XX.XX)	XX (XX.XX)
	Device issue resulted in an adverse event?	Yes	n (%)	XX (XX.XX)	XX (XX.XX)
		No	n (%)	XX (XX.XX)	XX (XX.XX)
	Nebulization 2		n (%$)	XX (XX.XX)	XX (XX.XX)
	----		n (%)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects in the safety population; n: The number of subjects in the specific category; %$: calculated using the number of subjects in the safety population as the denominator (n/(N)*100);
%: calculated using the number of subjects in the safety population who received the nebulization, excluding missing values, as the denominator (n/(N non missing)*100).
Most: Close contact with the face (and mouth and nose covered)most of the time (>75%); Half: Close contact with the face (and mouth and nose covered)approx. half of the time (25%-75%); Almost Not: Close contact almost not achieved (<25% of the time).

Table 14.3.1.1: Treatment-emergent adverse events: Summary Table (Safety Population)

Characteristic	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Subjects with at least one treatment-emergent adverse event (TEAE)	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one serious TEAE	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one TEAE leading to death	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one severe TEAE as classified by the investigator	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one TEAE for which the study drug was interrupted	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one TEAE for which the study drug or study was discontinued	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one TEAE that was considered treatment-related by the investigator	n (%)	XX (XX.XX)	XX (XX.XX)
Subjects with at least one serious TEAE that was considered treatment-related by the investigator	n (%)	XX (XX.XX)	XX (XX.XX)

TEAE: treatment-emergent adverse event.
N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).

Table 14.3.1.2: Treatment-emergent adverse events: Tabulation of all adverse events (Safety Population)

System Organ Class Preferred Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any adverse event	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class A	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class B	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
...			
...			

E: Number of events; N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.1.3: Treatment-emergent adverse events: Tabulation of all adverse events by severity (Safety Population)

System Organ Class Preferred Term	Severity	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any adverse event	Mild	n (%)	XX (XX.XX)	XX (XX.XX)
	Moderate	n (%)	XX (XX.XX)	XX (XX.XX)
	Severe	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)
System Organ Class A	Mild	n (%)	XX (XX.XX)	XX (XX.XX)
	Moderate	n (%)	XX (XX.XX)	XX (XX.XX)
	Severe	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)
Preferred Term 1	Mild	n (%)	XX (XX.XX)	XX (XX.XX)
	Moderate	n (%)	XX (XX.XX)	XX (XX.XX)
	Severe	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)
System Organ Class B	Mild	n (%)	XX (XX.XX)	XX (XX.XX)
	Moderate	n (%)	XX (XX.XX)	XX (XX.XX)
	Severe	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)
Preferred Term 1	Mild	n (%)	XX (XX.XX)	XX (XX.XX)
	Moderate	n (%)	XX (XX.XX)	XX (XX.XX)
	Severe	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.1.4: Treatment-emergent adverse events: Tabulation of serious adverse events (Safety Population)

System Organ Class Preferred Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any serious adverse events	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class A	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class B	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
...			
...			

E: Number of events; N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.1.5: Treatment-emergent adverse events: Tabulation of all adverse events by relationship to study drug (Safety Population)

System Organ Class Preferred Term	Causality	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any adverse event	Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Possible Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Unlikely Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Applicable	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX)	XX (XX.XX)
System Organ Class A	Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Possible Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Unlikely Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Applicable	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Possible Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Unlikely Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Related	n (%)	XX (XX.XX)	XX (XX.XX)
	Not Applicable	n (%)	XX (XX.XX)	XX (XX.XX)
	Missing	n (%)	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	Related	n (%)	XX (XX.XX)	XX (XX.XX)
...	Possibly Related	n (%)	XX (XX.XX)	XX (XX.XX)

N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.1.6: Treatment-emergent adverse events: Tabulation of the events for which the study drug was discontinued (Safety Population)

System Organ Class Preferred Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any adverse event	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class A	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class B	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
...			
...			

E: Number of events; N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.1.7: Treatment-emergent adverse events: Tabulation of non-serious adverse events (Safety Population)

System Organ Class Preferred Term	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Any serious adverse events	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class A	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
System Organ Class B	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 1	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 2	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
Preferred Term 3	n (%) E	XX (XX.XX) XX	XX (XX.XX) XX
...			
...			

E: Number of events; N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects in the safety population as the denominator (n/N*100).
All adverse events are coded using MedDRA version 20.0.

Table 14.3.2.1: Laboratory data: Descriptive statistics of the actual values and changes from baseline per time point (Safety Population)

Laboratory test (unit)

		Result						Change from baseline					
Treatment Group	Scheduled day/ time	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
XXXXX	Baseline	X	XX	XX	XX	XX	XXX						
	Follow-up	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
---	...	X	XX	XX	XX	XX	XXX						

Max = maximum; Min: minimum; SD: standard deviation.
Baseline is defined as the last observation prior to first study drug administration.

Note to Programmer: Each lab test on a new page; table sorted first by treatment group then time point.

Treatment groups are; Placebo, ALX-0171 1.5 mg

Table 14.3.2.2: Laboratory data: Cross-tabulation of the worst-case abnormalities (Safety Population)

Laboratory test (unit)

Treatment Group	Baseline	Worst Post-Baseline Value					
		Abnormal Low n (%)	Normal n (%)	Abnormal High n (%)	Abnormal Low+High n (%)	Not Available n (%)	Total n (%)
XXXXX	Abnormal Low	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Normal	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Abnormal High	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Not Available	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Total	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	N (100.00)
---	Abnormal Low	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Normal	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Abnormal High	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Not Available	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)
	Total	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	XX (XX.XX)	N (100.00)

N: number of subjects in the safety population; %: number of subjects in each category expressed as a percentage of N.
Baseline is defined as the last observation prior to first study drug administration.

Note to Programmer: Each lab test on a new page; Table sorted first by treatment group

Treatment groups are; Placebo, ALX-0171 1.5 mg

Table 14.3.3.1: Vital signs: Descriptive statistics of the actual values and changes from baseline per time point (Safety Population)

Test: Vital sign parameter (unit)

		Result						Change from baseline					
Treatment Group	Scheduled day/ time	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
Xxxxxx	Baseline	X	XX	XX	XX	XX	XXX						
	Day x	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
	...	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
	Follow-up	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
...	...	X	XX	XX	XX	XX	XXX						

Max = maximum; Min: minimum; SD: standard deviation.
Baseline is defined as the last observation prior to first study drug administration.

Note to Programmer: Each parameter on a new page; Table sorted first by treatment group and then by time point.
Please display the following variables; temperature (°C), weight (kg), heart rate (HR) (bpm), blood oxygen (Sp02) level (%), and duration of oxygen supplementation (hours)
Please display duration of oxygen supplementation (hours) at the end (the lastest test) and erase Schedule day/time and change from baseline columns as not needed.

Table 14.3.3.2: Vital signs: Tabulations per time point (Safety Population)

Test: XXXXXX

			Observed Value	
Time Point	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
(Baseline)	XXX	n (%)	XX (XX.XX)	XX (XX.XX)
	XXX	n (%)	XX (XX.XX)	XX (XX.XX)
	----	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXX	XXX	n (%)	XX (XX.XX)	XX (XX.XX)
	XXX	n (%)	XX (XX.XX)	XX (XX.XX)
	----	n (%)	XX (XX.XX)	XX (XX.XX)
XXXXXX	XXX	n (%)	XX (XX.XX)	XX (XX.XX)
	XXX	n (%)	XX (XX.XX)	XX (XX.XX)

N: number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects with non missing data in the safety population for the applicable treatment group as the denominator (n/(N non missing)*100).
Baseline is defined as the last observation prior to first study drug administration.

Note to Programmer: Each parameter on a new page; Table sorted first by test, then by time point.
Please display the following variables;Hear Rate collection method, Location of Sp02 measurement, Oxygen flow delivered (yes/no)

Table 14.3.4.1: RDA: Descriptive statistics of the actual values and changes from baseline in respiratory rate per time point (Safety Population)

Test: XXXXXX

		Result						Change from baseline					
Treatment Group	Scheduled day/ time	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
XXXXX	Baseline	X	XX	XX	XX	XX	XXX						
	Day x	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
	...	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
	Follow-up	X	XX	XX	XX	XX	XXX	X	XX	XX	XX	XX	XX
...	...	X	XX	XX	XX	XX	XXX						

Max = maximum; Min: minimum; SD: standard deviation.
Baseline is defined as the last observation prior to first study drug administration.

Note to Programmer: Each test on a new page; Table sorted first by treatment group and then by time point.

Table 14.3.4.2: RDA: Tabulations per time point (Safety Population)

Test: XXXXXXX

Time Point	Category	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Baseline				
	XXXXXXXX	n(%)	X (XX.X%)	X (XX.X%)
	XXXXXXXXXX	n(%)	X (XX.X%)	X (XX.X%)
	XXXXXXXX	n(%)	X (XX.X%)	X (XX.X%)
	XXXXXXXX	n(%)	X (XX.X%)	X (XX.X%)

N: number of subjects in the safety population; n: The number of subjects in the specific category; %:calculated using the number of subjects with non missing data in the safety population as the denominator (n/(N non missing)*100).
Baseline is defined as the last observation prior to first drug administration.

Note to Programmer: Each test on a new page; Table sorted first by test, then by time point
Please display the following variables; lung auscultation (wheezing during expiration and inspiration, lung fields affected by wheezing, crackles/crepitations), repiratore muscle retractions (supraclavicular, intercostal, subcostal), daytime coughing and night-time coughing.

Table 14.3.5.1: Duration of hospitalization: tabulation (Safety Population)

Parameter	Statistic	Placebo (N = XX)	ALX-0171 1.5 mg (N = XX)
Hospitalization (discharge)			
Events	n (%)	XX (XX.XX)	XX (XX.XX)
Censored	n (%)	XX (XX.XX)	XX (XX.XX)
Median Time to discharge (days)		XX	XX
95% CI		(XX.X, XX.X)	(XX.X, XX.X)
Duration of Hospitalization (days)	n	XX	XX
	Mean	XX.X	XX.X
	SD	XX.XX	XX.XX
	Minimum	XX	XX
	Maximum	XX	XX

SD: standard deviation; CI: Confidence interval
N: The number of subjects in the safety population; n: The number of subjects in the specific category; %: calculated using the number of subjects with non missing data in the safety population as the denominator (n/(N non missing)*100).

15.2 Mock Listings

Listing 16.2.1.1: Subject Disposition (All screened subjects)

Subject Number/Site	Date of ICF	Randomization group	Date of Randomization	Randomization number	Treatment actually received*	Analysis population Safety
XXX/X		Placebo			Placebo	<YES>

All discrepancies between randomization and treatment group will be flagged.

Note to Programmer: Table sorted first by randomization group and then by subject ID.

Listing 16.2.1.2: Demographics (Safety Population)

Treatment Group: XXXXXX

Subject Number/ Site	Date of ICF	Date of Randomization	Gestional Ages (weeks)	Age (month)	Gender	Ethnic Origin	Race	Asian	Height (cm)	Weight (kg)	Weight Category (kg)	Atopy History	Exposure to Tobacco	Exposure to Pets	Breast fed
XXX/X			XX	XX	MALE	HISPANIC OR LATINO	WHITE								
XXX/X			XX	XX	FEMALE	NOT HISPANIC OR LATINO	ASIAN	XXXXX							

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.1.3: Baseline Characteristics (Safety Population)

Treatment Group: XXXXXX

				RSV Severity Criteria				
Subject Number/Site	Heart Rate (bpm) at Baseline	Blood Oxygen (SpO2) Level (%) at Baseline	Time since onset RSV Signs and Symptoms (days)	Inadequate Oral Feeding	Inadequate Oxygen Saturation	Respiratory Distress	Inadequate Oral Feeding and Inadequate Oxygen Saturation and Respiratory Distress	Inadequate Oral Feeding and Inadequate Oxygen Saturation

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.1.4: Medical History and Concomitant Diseases (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Body System	Description of Disease/Procedure	Start Date	End Date	Ongoing at screening
			DDMMMYYYY	DDMMMYYYY	<YES>

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.1.5: Prior and Concomitant Therapies (Safety Population)

Treatment Group: XXXXXX

Subject ID	verbatim	ATC Level 4 Class Preferred Term	Prior/ Concomitant	First study drug administration Date/Time	Start Date/Time	End Date/Time	Ongoing at the end of trial?	Reason for use	Indication	Dose (unit)	Dosing frequency
					YYYY-MM-DD /HH:MM	YYYY-MM-DD /HH:MM	<YES>				

Prior medications are medications that were given prior to date/time of informed consent and which ended before date of informed consent
Concomitant medications/oxygen supplementation therapies are medications/oxygen supplementation therapies which are ongoing at signing of informed consent or which started after the signing of informed consent

Listing 16.2.1.6: Exposure to Study Medication (Safety Population)

Treatment group : xxxx

Subject ID	Visit Day 1	Type of Nebulization	Nebulizer Fill Date/Time	Nebulizer Airflow Type	Study drug Initiated successfully ? Yes/No (If No, specify reason)	Date/Time of start Date/Time of end	Was the administration fully done?	Was the inhalation period interrupted? Yes/No (If Yes, specify times)	Contact with Face Mask?	Resistance to study drug administration	Crying during Nebulization?	Did any problem occur during use of the device?	Did this device issue result in an adverse event?

Note to Programmer: Table sorted first by treatment group and then by subjectID, visit, and nebulization.

Listing 16.2.2.1: Adverse events (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Start and Stop Date/Time of each nebulization	AE Description (verbatim)	1. MedDRA System Organ Class 2. MedDRA Preferred Term	1. Start Date/Time 2. End Date/Time 3. Ongoing	1. Onset Day 2. Duration (days)	1. Severity 2. Drug relatedness 3. Relatedness to study procedure 4. Outcome	1. Action Taken 2. Concomitant Therapy 3. Seriousness
						<mild>	
				DDMMMYYYY/HH:MM		<not related>	<action taken>
			SOC	DDMMMYYYY/HH:MM	Day X	<not related>	<Yes/No>
			PT	<Yes/No>	X	<outcome>	<seriousness>

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; TEAE: treatment emergent adverse event.
*: AE is considered Serious; &: AE is considered TEAE.
All adverse events are coded using MedDRA version 20.0.

Note to Programmer:
If AE is Serious, add an "*" to the Description; If AE is TEAE, add an "&" to the Description
Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.2.2: Serious Adverse events (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Start and Stop Date/Time of each nebulization	AE Description	1. MedDRA System Organ Class 2. MedDRA Preferred Term	1. Start Date/Time 2. End Date/Time 3. Ongoing	1. Onset Day 2. Duration (days)	1. Severity 2. Drug relatedness 3. Relatedness to study procedure 4. Outcome	1. Action Taken 2. Concomitant Therapy 3. Seriousness
						<mild>	
				DDMMMYYYY/HH:MM		<not related>	<action taken>
			SOC	DDMMMYYYY/HH:MM	Day X	<not related>	<Yes/No>
			PT	<Yes/No>	X	<outcome>	<seriousness>

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; TEAE: treatment emergent adverse event.
&: AE is considered TEAE.
All adverse events are coded using MedDRA version 20.0.

Note to Programmer:
If AE is TEAE, add an "&" to the Description
Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.2.3: Adverse events leading to study drug discontinuation (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Start and Stop Date/Time of each nebulization	AE Description	1. MedDRA System Organ Class 2. MedDRA Preferred Term	1. Start Date/Time 2. End Date/Time 3. Ongoing	1. Onset Day 2. Duration (days)	1. Severity 2. Drug relatedness 3. Relatedness to study procedure 4. Outcome	1. Action Taken 2. Concomitant Therapy 3. Seriousness
						<mild>	
				DDMMMYYYY/HH:MM		<not related>	<action taken>
			SOC	DDMMMYYYY/HH:MM	Day X	<not related>	<Yes/No>
			PT	<Yes/No>	X	<outcome>	<seriousness>

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; TEAE: treatment emergent adverse event.
*: AE is considered Serious; &: AE is considered TEAE.
All adverse events are coded using MedDRA version 20.0.

Note to Programmer:
If AE is Serious, add an "*" to the Description; If AE is TEAE, add an "&" to the Description
Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.2.4: Adverse events leading to death (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Start and Stop Date/Time of each nebulization	AE Description	1. MedDRA System Organ Class 2. MedDRA Preferred Term	1. Start Date/Time 2. End Date/Time 3. Ongoing	1. Onset Day 2. Duration (days)	1. Severity 2. Drug relatedness 3. Relatedness to study procedure 4. Outcome	1. Action Taken 2. Concomitant Therapy 3. Seriousness
						<mild>	
				DDMMMYYYY/HH:MM		<not related>	<action taken>
			SOC	DDMMMYYYY/HH:MM	Day X	<not related>	<Yes/No>
			PT	<Yes/No>	X	<outcome>	<seriousness>

AE: adverse event; MedDRA: Medical Dictionary for Regulatory Activities; SAE: serious adverse event; TEAE: treatment emergent adverse event.
*: AE is considered Serious; &: AE is considered TEAE.
All adverse events are coded using MedDRA version 20.0.

Note to Programmer:
If AE is Serious, add an "*" to the Description; If AE is TEAE, add an "&" to the Description
Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.3.1: Laboratory data: Abnormalities (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Lab Test (Unit)	Visit/ Time Point	Date/Time of Measurement	Result (a,b)	Change From Baseline	Reference Range Low - High
XX/XX	XXx	Baseline	DDMMMYYYYThh:mm	XX.X (AH, ncs)		XX.X - XX.X
		Follow-up	DDMMMYYYYThh:mm	XX.X (AL, cs)	XX.X	XX.X - XX.X

a: AH = Abnormally High, AL = Abnormally Low, N = Normal; b: NCS = not clinically significant, CS = clinically significant.
Baseline is defined as the last observation prior to first drug administration.

Note to Programmer: Table sorted first by treatment group and then by subject number. Present lab data from all visits from a subject with at least one abnormality

Listing 16.2.4.1: Duration of Hospitalization (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	1.- Date/Time of Admission 2.- Ongoing at the End of the Trial	Date/Time of Discharge	Duration of Hospitalization (days)	Was Subject Admitted to the ICU?
XX/XX	DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM		Yes/No

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.4.2: Duration of ICU (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	1.Date/Time of Admission 2.Ongoing at the End of the Trial	Date/Time of Discharge	Duration of ICU (days)
XX/XX	DDMMMYYYY/HH:MM	DDMMMYYYY/HH:MM	

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.4.3: Apnea and ventilation (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Date/Time of Apnea	Was ventilation required	Start Date/Time of Ventilation	End Date/Time of Ventilation	1. Ventilation Type 2. If Non-Invasive Respiratory Support (specification)
XX/XX	DDMMMYYYY/HH:MM	<Yes/No>			

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.5.1: Physical examination: Abnormalities (Safety Population)

Treatment Group: XXXXXX

Subject Number/Site	Visit/ Timepoint	Date/time of Assessment	Body System	Result	Details of Abnormality
		DDMMMYYYY/HH:MM		ABNORMAL (NCS)	

CS: clinically significant; NCS: not clinically significant.

Note to Programmer: Table sorted first by treatment group and then by subject number

Listing 16.2.6.1: Viral Load (Safety population)

Treatment Group: XXXXXX

Subject ID	Visit/ Time Point	Date/time of sample collection	Collection(from both nostrils, right or left)	Plaque Assay Result (unit)	RT-qPCR Result (unit)
XX/XX				XX.X	XX.X
				XX.X	XX.X

Note to Programmer: Table sorted first by treatment group and then by subject ID.

Listing 16.2.7.1: Study Drug Concentrations and Sampling Times (Safety Population)

Treatment Group: XXXXXX

Subject ID	Nominal Time Point	Actual blood sampling data/time	Second study drug administration date/time	Actual Sampling Time Relative to second study drug administration (hours)	Concentration (unit)
XX/XX				XX	

Note to Programmer: Table sorted first by treatment group and then by subject ID.

Listing 16.2.8.1: Immunogenicity – Full Data (Safety Population)

Treatment Group: XXXXXX

			ADA Assay		NAb Assay	
Subject ID	Visit/ Time Point	Date/time of sample collection	Subject classification	ADA log_{10} (titer)	Subject classification	NAb result
XX/XX						

All samples confirmed positive in the ADA assay will be further characterized in the NAb assay. Subjects with no positive ADA samples, will not be analyzed in the NAb assay and will be classified as pre-dose NEG – NEG on treatment.
NAb assay results will be reported as values (ratio is optical density (OD) value over negative control (NC)).

Note to Programmer: Table sorted first by treatment group and then by subject ID.