Protocol C5241009

AN INTERVENTIONAL, PHASE 1b, RANDOMIZED, DOUBLE-BLIND, SPONSOR-OPEN, PLACEBO-CONTROLLED, MULTI-CENTER, DOSE-FINDING STUDY TO EVALUATE SAFETY, TOLERABILITY AND PHARMACOKINETICS OF SISUNATOVIR IN PEDIATRIC PARTICIPANTS UP TO AGE 60 MONTHS WITH RESPIRATORY SYNCYTIAL VIRUS (RSV) LOWER RESPIRATORY TRACT INFECTION (LRTI)

Statistical Analysis Plan (SAP)

Version: V3.0

Date: 28 Feb 2025

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APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
3 28 Feb 2025	Final Protocol Amendment 4, 11 Mar 2024 PACL 11, 19 Apr 2024	Hyperlinking updates	Section 2: Updated section numbers Section 3.2.1: Updated hyperlinking.
2 04 Oct 2024	Final Protocol Amendment 4, 11 Mar 2024 PACL 11, 19 Apr 2024	Removal of ECG and palatability as endpoints. Additional clarifications, definitions, and outputs required.	Section 2: Edited for clarity. Removed palatability. Section 2.2: Removed ECG from the primary endpoints. Removed palatability objective and endpoint. Added treatment duration. Section 3.1: Removed ECG from the primary endpoints. Section 3.1.3: Removed the definition and convention of ECG. Section 3.1.3.2: Added Oxygen saturation (SpO_2) to the vital sign endpoints and removed the specifications of post-baseline days. Section 3.2: Removed the statements of efficacy and safety endpoints. Section 3.3: Added description of ECG data. Section 3.4: Removed palatability. Section 3.4.1: Edited for clarity. Section 3.4.2: Added duration of signs and symptoms. Section 3.5: Edited for clarity. Section 5.2: Edited for clarity. Section 5.3: Added clarifications of viral loadlisting.

			Section 6.1.3: Removed analyses and summaries of ECG. Section 6.1.3.2: Removed the summary of vital signs by categorial criteria and clarified output of SpO_2. Section 6.2: Removed the statements on efficacy and safety endpoints. Section 6.2.1: Added clarifications of nominal time. Section 6.4: Removed palatability. Section 6.4.1: Added more analyses on viral load. Section 6.4.2: Added more analyses on RSV signs and symptoms. Section 6.6.1: Added more analyses of baseline characteristics. Section 6.6.4: Removed the summary of maternal RSV vaccine. Appendix 1: Removed the categories for ECG and vital signs. Appendix 2: Updated abbreviations.
1 30 Oct 2023	Final Protocol Amendment 2, 13 Sept 2023 PACL 3 20 Sept 2023	N/A	N/A

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study C5241009.

Sisunatovir (PF-07923568, formerly RV521) is a potent inhibitor of respiratory syncytial virus *(RSV) F protein mediated cell-to-cell fusion that is currently being investigated in participants with RSV LRTI.*

The purpose of this study is to establish safety, tolerability, PK and guidance for dosing of sisunatovir in a pediatric population (1 day up to 60 months of age) with RSV-LRTI for further clinical development of sisunatovir. This study will provide additional safety, tolerability and PK data at ages previously evaluated in C5241003 to inform dose selection

in future studies and will also provide this data in a broader pediatric population to inform dose selection in future studies.

2.1. Modifications to the Analysis Plan Described in the Protocol

None. There are no changes to the analysis described in the protocol.

2.2. Study Objectives, Endpoints, and Estimands

Type	Objective	Endpoint
	Primary:	***Primary:***
Safety (Section 6.1)	*To evaluate the safety and tolerability of sisunatovir compared to placebo in participants with RSV-LRTI.*	• *Incidence of TEAEs.* • *Incidence of AEs and SAEs leading to discontinuations.* • *Incidence of clinically significant abnormal laboratory values and vital signs.*
	Secondary:	***Secondary:***
PK (Section 6.2.1)	*To characterize the PK of sisunatovir in participants with RSV-LRTI.*	• *Plasma concentrations of sisunatovir at steady state (Day CCI or later).*
	Tertiary:	***Tertiary:***
Other - Virological response (Section 6.4.1)	*To describe the viral load in* Nasopharyngeal (NP) *samples over time in participants with RSV-LRTI.*	• *Viral load measured via RT-qPCR in NP swabs over time (including but not limited to change from baseline at each sampled visit and proportion of participants with BLOQ at Day CCI*
Efficacy (Section 6.4.2)	*To describe signs and symptoms assessed by HCP over time in participants with RSV-LRTI*	*Signs and symptoms over time (including but not limited to change from baseline at Day CCI and proportion of participants with each sign at Day CCI)*
Other - Virological response (Section 6.4.3)	CCI [redacted]	• CCI [redacted] • *Viral load in NP swabs and RSV signs and symptoms over time in -participants* CCI [redacted]

There are no estimands for this study.

2.3. Study Design

This study is a randomized, double-blind, sponsor-open, placebo-controlled, multicenter study in RSV-infected outpatient and hospitalized neonates, infants and children, aged 1 day up to 60 months of age with RSV-LRTI; this is a dose finding study to evaluate the PK, safety and tolerability of sisunatovir.

CCI [redacted]

- *Cohorts 1 and 2:*

A: CCI [redacted]
B:
C:
D:

- *Cohort 3:*

E: CCI [redacted]
F:
B:
D:

Sisunatovir or placebo will be administered CCI *in a* CCI *ratio, for a period of* CCI [redacted] *for all cohorts.*

The sample size has been chosen empirically to provide safety and tolerability information and is not based on statistical power calculation.

CCI *participants (*CCI *active;* CCI *placebo) are planned for each* age band *so that approximately* CCI *evaluable participants (*CCI *per cohort) may be randomized into the study. The number randomized may be increased if Sponsor recommends repeating the dose for* an age band *(ie, an additional* CCI *active and* CCI *placebo may be enrolled in the same* age band*). This totals to approximately a maximum of 108 evaluable participants (*CCI *in each* age band + CCI *additional in each* age band *if necessary). The sample size for* age bands *may be reduced to* CCI CCI *active,* CCI *placebo) if there are enrollment challenges. The minimum number of participants is approximately* CCI *evaluable participants (based on* CCI *participants per* age band*) as Cohorts 2 (2A, 2B, 2C, 2D) and 3 (3E, 3F, 3B, 3D) are optional in the study. Participants may be replaced at Sponsor discretion. Participants who discontinue from the study for non-safety reasons may be replaced at the sponsor's discretion in collaboration with the Investigator.*

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoint(s)

The primary endpoints are related to safety/tolerability

- *Incidence of TEAEs.*
- *Incidence of AEs and SAEs leading to discontinuations.*
- *Incidence of clinically significant abnormal laboratory values and vital signs.*

3.1.1. Incidence of TEAEs

An AE is any untoward medical occurrence in a study participant administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. An AE is considered a Treatment-Emergent Adverse Event (TEAE) if the event started during the effective duration of treatment. All events that start on or after the first dose of study intervention, but before the end of the study will be flagged as TEAEs. The algorithm will not consider any events that started prior to the first dose date.

3.1.2. Incidence of AEs and SAEs leading to discontinuations

The definition of a serious adverse event is described in Appendix 3 of the protocol.

A participant who discontinues study intervention due to an AE or an SAE will be flagged.

3.1.3. Incidence of clinically significant abnormal laboratory values and vital signs.

3.1.3.1. Laboratory Data

The investigator must review the laboratory report, document this review, and record any clinically significant changes occurring during the study in the AE section of the CRF. Clinically significant abnormal laboratory test findings are those that are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.

To determine if there are any clinically significant laboratory abnormalities, the hematological and clinical biochemistry and other safety tests will be assessed against the criteria specified in the Pfizer reporting standards. This assessment will consider whether each participant's baseline test results are within or outside the laboratory reference range for particular laboratory parameter.

Baseline will be the last pre-dose measurement. Change from baseline (CFB) will be calculated for all post-baseline timepoints.

3.1.3.2. Vital signs

Vital signs measures will include blood pressure (BP), pulse rate (PR), Temperature (Tympanic, Rectal or Skin), respiratory rate (RR) and Oxygen saturation (SpO2). Baseline will be the last pre-dose measurement.

At times defined in the protocol SoA, a single measurement of BP and PR will be assessed with a completely automated device.

Temperature and the highest respiratory rate at the time of assessment will be recorded.

Oxygen saturation findings collected during the study will be recorded on the CRF including any supplemental O2 requirement. The lowest SpO2 value, while on room air at the time of assessment will be documented.

The following endpoints will be determined:

- Change from baseline in systolic and diastolic BP, pulse rate, temperature, respiratory rate, and SpO2.
- The minimum and maximum post-dose systolic and diastolic BP, pulse rate, temperature, respiratory rate, and SpO2.
- The maximum increase and decrease from baseline over all measurements taken post-dose for systolic and diastolic BP, pulse rate, temperature, respiratory rate, and SpO2 values.

The maximum increase from baseline will be calculated by selecting the maximum CFB over the respective period, except in the case where a participant does not show an increase. In such an instance, the minimum decrease should be taken. Similarly, the maximum decrease from baseline will be determined by selecting the minimum value of the CFB. In cases where a participant does not show a decrease, the minimum increase should be taken.

3.2. Secondary Endpoint(s)

3.2.1. Pharmacokinetic (PK) Endpoints

To calculate plasma concentrations of sisunatovir at steady state, blood samples will be taken on Day [redacted] pre-dose, [redacted] post dose and pre dose on Day [redacted]. If post-dose PK samples are not collected on Day [redacted], they will be collected on Day [redacted] For the purposes of plasma concentration summaries, the nominal day of the sample will be used.

3.3. Other Safety Endpoint(s)

Medical history and physical examination and neurological examination information, as applicable, collected during the course of the study, will be considered source data and will not be required to be reported, unless otherwise noted. However, any untoward findings identified on physical and/or neurological examinations conducted during the active collection period will be captured as AEs, if those findings meet the definition of an AE.

A single ECG will be collected at screening, and as specified in the SoA. ECG may be performed after screening as needed per investigator discretion. Any clinically significant ECG abnormalities that meet the definition of an AE will be captured as AEs.

3.4. Other Endpoint(s) (or, Exploratory Endpoints)

3.4.1. Viral Load

Viral load will be measured in NP swabs. Samples will be analyzed to measure RSV A and B RNA levels by reverse transcription polymerase chain reaction (RT-qPCR). For each participant and visit, the numeric viral load value will be the sum of that from subtype A and subtype B, followed by $\log_{10}$ transformation for analysis.

Baseline will be measured pre-dose on Day 1. Change from baseline in viral load will be calculated at each sampled visit.

For viral load summaries, numeric log10 copies/mL values will be derived from the possible categorical results as follows:

- If the result is 'TND' (target not detected <LOD), a value of 0 log_{10} copies/mL will be used, as applicable for both subtype A and B.
- If the result is 'TD' (target detected <LLOQ), the midpoint between the unlogged LLOQ and LOD will be used, ie, a value of 2.91 log_{10} copies/mL will be used for subtype A (converted from a midpoint of 810 copies/mL) and 2.22 log_{10} copies/mL for subtype B (converted from a midpoint of 165 copies/mL).
- If the result is '>ULOQ', a value of 9 log_{10} copies/mL will be used, as applicable for both subtype A and B. Such values may ultimately be replaced by numeric results in subsequent data transfers.

Undetectable RSV viral load is defined as a central PCR laboratory result of 'TND' (or, a converted numeric value of 0 log_{10} copies/ml) for both subtype A and subtype B.

3.4.2. RSV Signs and Symptoms

RSV associated signs and symptoms will be assessed (as present/not present) by HCP (Appendix 10A of Protocol). The pre-dose assessment on Day 1 will be considered the baseline. Further assessments will be made over time with hospitalized patients assessed daily. Each sign and symptom will be analyzed separately.

Durations of RSV signs and symptoms at baseline will be determined. Duration at baseline is calculated as: baseline date – onset date + 1.

3.4.3. CCI

CCI [redacted]

3.5. Baseline Variables

Baseline values will be the last value recorded prior to starting study treatment unless otherwise specified.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database and classifications will be documented per standard operating procedures.

Participant Analysis Set	Description
Enrolled	*"Enrolled" means a participant's, or their parent(s)/legal guardian's, agreement to participate in a clinical study following completion of the informed consent process and randomization.*
Full analysis set	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention.*

Safety analysis set	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention. Participants will be analyzed according to the product (sisunatovir / placebo) they actually received.*
PK Concentration Population	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention and in whom at least 1 concentration value can be reported.*
PK Parameter Analysis Population	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention and in whom at least 1 of the PK parameters of interest can be reported*
Biomarker Analysis Population	*All participants randomly assigned to study intervention and who take at least 1 dose of study intervention and in whom at least 1 of the measured parameters of interest can be reported.*

5. GENERAL METHODOLOGY AND CONVENTIONS

Final analysis will be performed after study participant data set release following the last participant last visit.

5.1. Hypotheses and Decision Rules

There are no statistical hypotheses for this study.

5.2. General Methods

The analyses related to the primary and secondary endpoints will be based on the appropriate population for analysis (see Section 4).

Unless otherwise stated, all summaries and plots will be presented by treatment group, by cohort and age band (if data permits), and overall, if applicable. The following treatment group labels (or similar) will be used:

- Placebo
- Sisunatovir

Cohorts and age bands are as follows:

- Cohort 1A: CCI
- Cohort 1B:
- Cohort 1C:
- Cohort 1D:
- Cohort 2A:
- Cohort 2B:
- Cohort 2C:

- Cohort 2D: CCI [redacted]
- Cohort 3E:
- Cohort 3F:
- Cohort 3B:
- Cohort 3D:

Some measures will be summarized using graphical representations.

5.2.1. Analyses for Continuous Endpoints

For continuous endpoints, the data will be summarized using number of participants, arithmetic mean, standard deviation (SD), median and range (minimum and maximum) in accordance with the sponsor reporting standards. For variables to be analyzed on the natural log scale ($\log_e$) or base 10 log scale ($\log_{10}$), the geometric mean and geometric coefficient of variation (%CV) will additionally be calculated.

5.2.2. Analyses for Binary/Categorical Endpoints

For binary or categorical endpoints, number of participants, numbers and percentages of participants meeting the categorical criteria will be presented in accordance with the sponsor reporting standards.

For the endpoints of signs and symptoms, a shift table of number of participants with and without a sign/symptom at Day CCI [redacted] against baseline will be summarized for each sign/symptom separately. The proportion of participants with signs and symptoms will also be reported and plotted over time.

5.3. Methods to Manage Missing Data

For the analysis of safety endpoints, the sponsor data standard rules for imputation will be applied.

In all PK data presentations (except listings), concentrations below the limit of quantification (BLOQ) will be set to zero.

In listings, BLOQ values (for PK or PD) will be reported as "<LLOQ", where LLOQ will be replaced with the value for the LLOQ.

In listings of viral load, BLOD values will be reported as "TND" and BLOQ values will be reported as "TD".

For PK and PD summary tables and plots of median profiles, statistics will be calculated having set concentrations to missing if one of the following cases is true:

1. A concentration has been collected as ND (i.e., not done) or NS (i.e., no sample)
2. A deviation in sampling time is of sufficient concern or a concentration has been flagged anomalous by the pharmacokineticist/statistician.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint(s)

All analyses of primary endpoints (safety analyses) will be performed on the safety population defined in Section 4.

6.1.1. Incidence of TEAEs

The incidence of TEAEs will be tabulated by cohort, age band and treatment.

6.1.2. Incidence of AEs and SAEs leading to discontinuations

The incidence of AEs and SAEs leasing to discontinuation will be tabulated by cohort, age band and treatment. The safety analysis set will be used.

6.1.3. Incidence of clinically significant abnormal laboratory values, and vital signs.

Any clinical laboratory and vital signs *abnormalities of potential clinical concern will be described. Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate.*

6.1.3.1. Laboratory values

Safety laboratory data will be listed and summarized by treatment group, cohort and age band and overall, in accordance with the sponsor reporting standards using the safety analysis set defined in Section 4. Baseline is as defined in Section 3.1.3.1. Data collected at screening that are used for inclusion/exclusion criteria, will be considered source data, and will not be required to be reported, unless otherwise noted.

6.1.3.2. Vital Signs

Absolute values and CFB in systolic and diastolic BP, pulse rate, temperature respiratory rate, and SpO_2 will be listed and summarized by cohort, age band, treatment and timepoint, according to sponsor reporting standards, using the safety analysis set defined in Section 4. Baseline is as defined in Section 3.1.3.2.

Mean absolute values and CFB for systolic and diastolic BP, pulse rate, temperature, respiratory rate, and SpO_2 will be plotted against time point. On each plot there will be one line for each cohort and age band with all treatments on the same plot. Corresponding individual plots of changes from baseline will also be produced for each treatment.

Maximum increase and decrease from baseline over all measurements taken post-dose for systolic and diastolic BPs, pulse rate, temperature respiratory rate, and SpO_2 will be summarized by cohort, age band and treatment, according to sponsor reporting standards.

6.2. Secondary Endpoint(s)

6.2.1. Pharmacokinetic analysis

The plasma concentrations of sisunatovir will be listed and descriptively summarized by nominal PK sampling time, treatment, age group, and cohort. Individual participant and summary profiles (mean and median plots) of the plasma concentrations data will be plotted

by treatment, cohort and age group using actual and nominal times, respectively. Mean and median profiles will be presented on both linear and semi-log scales.

Nominal time recorded as 2H post dose corresponds to CCI post dose and nominal time recorded as 6H post dose corresponds to CCI post dose. When nominal time is CCI post dose, 54 min – 132 min is within 10% nominal time. When nominal time is CCI post dose, 216 min – 396 min is within 10% nominal time. The following will be presented for the plasma concentration data using the PK Concentration Set if data permits (as defined in Section 4):

- For each cohort and age band, a listing of all concentrations sorted by participant ID and nominal time post-dose. The concentration listing will also include the actual times. Deviations from the nominal time will be given in a separate listing.

- For each cohort and age band, a summary of concentrations by each nominal time post-dose, where the set of statistics will include n, mean, median, standard deviation, coefficient of variation (cv), minimum, maximum and the number of concentrations above the lower limit of quantification.

- median concentration time plots (on both linear and semi-log scales) against nominal time post-dose. One plot for each scale will be presented, which will include all cohorts and age bands in the same plot.

- individual concentration time plots by cohort and age band (on both linear and semi-log scales) against actual time post-dose (there will be separate spaghetti plots for each cohort and age band, with a line for each participant per scale).

- individual concentration time plots by participant (on both linear and semi-log scales) against actual time post-dose.

The nominal PK sampling time will be used for summary statistics and relevant median plots, whereas for individual participant plots by time, the actual PK sampling time will be used.

The final population PK model will be used to simulate plasma concentration-time curves for sisunatovir for individuals and to calculate post-hoc estimates of PK parameters (CL/F, C_{max}, C_{min}, AUC and $t_{½}$) by age group.

Data permitting, geometric means of PK parameters estimated from the final population PK model will be summarized descriptively by treatment and age group. A stand-alone population PK modeling and simulation analysis plan will be prepared, and the results will be reported in a stand-alone report, outside of the clinical study report.

6.3. Other Safety Summaries and Analyses Endpoint(s)

None.

6.4. Other Endpoint(s) (or, Exploratory Endpoint[s])

6.4.1. Viral load

Absolute values and change from baseline in log_{10} total RSV viral load by RT-qPCR will be summarized descriptively at each sampled visit by treatment, cohort, and age band, as described in Section 5.2.1. No imputation of missing data is planned. The absolute values and change from baseline in log_{10} total RSV viral load by RT-qPCR at each timepoint will also be listed for each participant.

A spaghetti plot of viral load values over time (by visit) will also be produced, differentiating participants from each treatment group. The number and proportion of participants with TND and TD, RSV viral load at each sampled visit will be presented respectively by treatment, cohort, and age band as described in Section 5.2.2.

6.4.2. RSV Signs and Symptoms

A summary table will be presented to show the number and proportion of participants, by treatment, cohort and age band, with each sign/symptom of RSV listed in Appendix 10A of the protocol and RR and SpO_2, at each timepoint as described in Section 5.2.2.

In addition, shift tables will be presented by treatment, cohort and age band for each sign/symptom, at baseline and Day [redacted] as described in Section 5.2.2.

Duration of the RSV signs and symptoms for each participant will be plotted using swimmer plots, with the x-axis ranging from the onset of symptoms prior to the start of the study or the start of the study, whichever is earlier.

6.4.3. [redacted]

[redacted]

6.5. Subset Analyses

None.

6.6. Baseline and Other Summaries and Analyses

6.6.1. Baseline Summaries

Demographic characteristics collected at screening will be summarized for the enrolled population in accordance with the sponsor reporting standards.

Data on premature birth and social factors collected at screening and during the study will be listed.

The number and percentages of participants infected with strain A, or B, or dual infected with A and B of RSV at baseline (pre-dose 1 swab) will be summarized. The number and percentages of participants with co-infections at baseline will also be summarized.

The number and percentage of participants who are inpatients (hospitalised) and outpatients at baseline, the duration of RSV symptoms at baseline, and whether on oxygen support at baseline will be summarized by cohort, treatment and age band.

The number and percentage of discrepancies between RSV diagnostic test results and Day 1 pre-dose NP swab results will be summarized by cohort, treatment and age band if applicable.

6.6.2. Study Conduct and Participant Disposition

Participants evaluation groups will show end of study participant disposition. Frequency counts will be supplied for participant discontinuation(s) by treatment. Data will be reported in accordance with the sponsor reporting standards.

6.6.3. Study Treatment Exposure

Duration of treatment will be summarized using safety analysis set.

The duration of treatment will be calculated as follows: Duration of treatment = Date of last dose of study drug - date of first dose of study drug +1.

6.6.4. Concomitant Medications and Nondrug Treatments

All concomitant medication(s) as well as non-drug treatment(s) will be reported in the listings according to current sponsor reporting standards.

The number and percentage of participants who have received niresvimab will be summarized descriptively as described in Section 5.2.2 by treatment, cohort, and age band.

6.6.5. Study Treatment Compliance

The number of syringes draws that are completely given, partially given, or not given for each dose administration will be listed. If the data is missing at a dose administration, it is considered not given.

The percentages of complete, partial, and none syringe draws for each participant are calculated as the total number of complete, partial, and none syringe draws during the treatment period divided by the total number of planned syringe draws during the treatment period. To assess compliance, the percentages will be summarized descriptively as described in Section 5.2.1 by treatment, cohort, and age band.

6.6.6. Other Exploratory Biomarkers

Biomarker data collected during the trial may be retained for future analyses. The results of biomarker analyses (except Viral RNA titres) are not planned to be included in the CSR.

6.6.7. Social Factors

The number of missed days of work since the start of RSV infection and during the study for parent(s) or legal guardians(s) due to the participant illness and the number of missed daycare days by the participant since the start of RSV infection and during the study will be summarized descriptively as described in Section 5.2.1 by treatment, cohort, and age band.

6.6.8. Medically Attended Visit

The total number of all outpatient visits, the number of emergency room visits, and the number of urgent care visits for each patient will be summarized descriptively as described in Section 5.2.1 by treatment, cohort, and age band.

The number and percentage of participants who have been hospitalized post-randomization, will be summarized descriptively as described in Section 5.2.2 by treatment, cohort, and age band. The number and percentage of participants requiring inpatient stays and the number and percentage of participants with ICU stay will also be summarized descriptively as described in Section 5.2.2 by treatment, cohort, and age band.

7. INTERIM ANALYSES

No formal interim analysis will be conducted for this study. As this is a sponsor-open study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, facilitating eDMC reviews of the data, *facilitating PK/PD modeling for dose confirmation prior to opening the next age cohort, business decisions regarding future project planning and/or supporting clinical development. Data from each cohort of the study may be reported in an interim report should the Sponsor determine an interim report is warranted. All analysis will be descriptive in nature.*

8. REFERENCES

None

Appendix 1. Data Derivation Details

Appendix 1.1. Definition and Use of Visit Windows in Reporting

The following table defines the visit windows and labels to be used for reporting.

Target Visit Day	Window	Label
1	Day 1	Day 1
CCI		

These visit windows may be revised for analysis and reporting purpose when deemed appropriate.

Appendix 2. List of Abbreviations

Abbreviation	Term
AE	adverse event
AUC	area under the curve
BLOQ	below the limit of quantification
BP	blood pressure
CFB	change from baseline
C_{max}	maximum observed concentration
C_{min}	minimum observed concentration
CL/F	apparent clearance
CRF	case report form
CSR	clinical study report
CV	coefficient of variation
ECG	electrocardiogram
eDMC	External Data Monitoring Committee
HCP	health care professional; health care provider
HR	heart rate
ICU	Intensive care unit
LLOQ	lower limit of quantification
LRTI	lower respiratory tract infection
LOD	limit of detection
N/A	not applicable
ND	not done
NP	nasopharyngeal
NS	no sample
PACL	protocol administrative change letter
PD	pharmacodynamic(s)
PK	pharmacokinetic(s)
PR	pulse rate
QTcF	corrected QT (Fridericia method)
RR	respiratory rate
RSV	respiratory syncytial virus
RT-qPCR	reverse transcription polymerase chain reaction
SAE	serious adverse event
SAP	statistical analysis plan
SD	standard deviation
SOA	Schedule of activity

Abbreviation	Term
SOP	standard operating procedure
SpO_2	oxygen saturation
$t_{1/2}$	terminal elimination half life
TEAE	treatment emergent adverse event
TD	target detected
TND	target not detected
ULOQ	upper limit of quantification
VAP	virology analysis plan