STATISTICAL ANALYSIS PLAN

Study Title:	A Phase 2, Randomized, Multicenter, Double-blind, Placebo-controlled Study to Evaluate the Safety, Tolerability, Pharmacokinetics, and Efficacy of Obeldesivir in Participants From Birth to < 5 Years of Age With Respiratory Syncytial Virus (RSV) Infection
Name of Test Drug:	Obeldesivir (GS-5245)
Study Number:	GS-US-685-6883
Protocol Version (Date):	Protocol Original (27 September 2024); Protocol Amendment 0.1 (Japan) (17 February 2025)
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Analysis Plan Author(s):	PPD

CONFIDENTIAL AND PROPRIETARY INFORMATION

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LIST OF ABBREVIATIONS

AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BLQ	below the limit of quantitation
BMI	body mass index
CA	chronological age
CGI-C	Caregiver Global Impression of Change
CGI-S	Caregiver Global Impression of Severity
CI	confidence interval
CRF	case report form
CSR	clinical study report
DAIDS	Division of AIDS
DMC	data monitoring committee
eCRF	electronic case report form
EOS	end of study
EOT	end of treatment
ET	early termination
EQ-5D	EuroQoL (5 dimensions)
EQ-5D-5L	EuroQol (5 dimensions, 5 levels)
EQ-5D-Y	EuroQol-5 Dimension-child specific
EQ-5D-Y-3L	EuroQol-5 Dimension-child specific (3 levels)
FAPS	Full Analysis Positive Set
FAS	Full Analysis Set
GA	gestational age
GRCD	Gilead RSV Caregiver Diary
HCPGI-S	Health Care Professional Global Impression of Severity
HLT	high-level term
HRQoL	health-related quality of life
ID	identifier
IVT	infectious viral titer
LLOQ	lower limit of quantitation
LLT	lowest-level term
LOD	limit of detection
LOQ	limit of quantitation
N	number of participants
MAVs	medically attended visits
MedDRA	Medical Dictionary for Regulatory Activities
ODV	obeldesivir

PK	pharmacokinetic(s)
PMA	postmenstrual age
PT	preferred term
Q1, Q3	first quartile, third quartile
RSV	respiratory syncytial virus
SAP	statistical analysis plan
SCR	screening
SD	standard deviation
SE	standard error
SI (units)	international system of units
SOC	system organ class
SRT	safety review team
TE	treatment emergent
TEAE	treatment-emergent adverse event
TELA	treatment-emergent laboratory abnormality
TFLs	tables, figures, and listings
ULN	upper limit of normal
UTM	universal transport medium
VAS	visual analogue scale
WHO	World Health Organization
WPAI	Work Productivity and Activity Impairment

1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures, and listings (TFLs) in the clinical study report (CSR) for Study GS-US-685-6883. This SAP is based on the study protocol original dated 27 September 2024, study protocol administrative amendment 0.1 (Japan) dated 17 February 2025, and the electronic case report form (eCRF). The SAP will be finalized before database finalization. Any changes made after the finalization of the SAP will be documented in the CSR.

This study was terminated early; hence only the analyses outlined in this SAP will be performed.

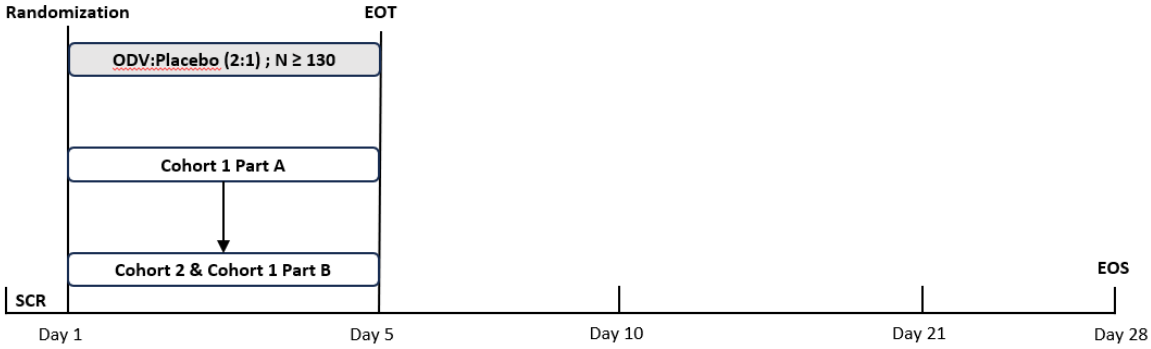
1.1. Study Objectives and Endpoints

Primary Objective(s)	**Primary Endpoint(s)**
• To evaluate the safety and tolerability of obeldesivir (ODV) in pediatric participants with respiratory syncytial virus (RSV) infection	• Proportion of participants experiencing treatment-emergent adverse events (TEAEs) by Day 28 • Proportion of participants experiencing Grade 3 or 4 treatment-emergent laboratory abnormalities (TELAs) by Day 28
• To evaluate the efficacy of ODV on duration of time until alleviation of targeted RSV symptoms in pediatric participants with RSV infection	• Time to alleviation of targeted RSV symptoms by Day 28
Secondary Objective(s)	**Secondary Endpoint(s)**
• To evaluate the plasma pharmacokinetics (PK) of ODV in pediatric participants with RSV infection	• PK parameters (AUC_{tau}, C_{max}, and C_{trough}) for ODV metabolite, GS-441524
• To evaluate the antiviral activity of ODV on RSV nasal swab viral load in pediatric participants with RSV infection	• Change from baseline in RSV nasal swab viral load at Day 5
• To evaluate the efficacy of ODV on duration of time until sustained alleviation of targeted RSV symptoms in pediatric participants with RSV infection	• Time to sustained alleviation of targeted RSV symptoms by Day 28
• To evaluate the efficacy of ODV on duration of time until resolution of targeted RSV symptoms in pediatric participants with RSV infection	• Time to resolution of targeted RSV symptoms by Day 28
• To evaluate acceptability and palatability of ODV in pediatric participants with RSV infection	• Assessment of palatability and acceptability scores of the age-specific formulation as assessed by caregiver at Days 1 and 5

1.2. Study Design

This is a Phase 2, randomized, multicenter, double-blind, placebo-controlled study comparing the safety, tolerability, PK, and efficacy of ODV with placebo for the treatment of RSV infection in participants from birth to < 5 years of age with and without risk factors for severe RSV disease. The study entry eligibility criteria are listed in Sections 4.2 and 4.3 of the study protocol.

Figure 1-1. Study Schema



EOS = end of study; EOT = end of treatment; N = number of participants; ODV = obeldesivir; SCR = screening
Screening window is within 48 hours of the Day 1 visit. Day 1 visit may occur the same day as screening.

At least 130 participants were planned to be randomized across 2 cohorts with a minimum of 24 participants for Cohort 2. Central randomization was implemented to minimize bias in the participant treatment assignment. As the study dosing regimen was defined based on weight groups, participants were divided into different weight groups within each cohort. Within each cohort/weight group, eligible participants were randomly assigned to receive ODV:placebo in a 2:1 ratio for 5 days.

This study was initially planned to enroll participants in Cohort 1 Part A. Enrollment in Cohort 2 and Cohort 1 Part B was planned to be initiated following a review of safety and available PK data by a safety review team (SRT) and a review of safety data by an external multidisciplinary data monitoring committee (DMC) after approximately 24 participants from Cohort 1 Part A have completed at least Day 5 assessments or prematurely discontinued the study. All cohorts were then planned to continue to enroll participants in parallel.

This study was terminated early, and the number of participants originally planned to be randomized was not achieved. The planned SRT and DMC reviews were not conducted.

Table 1-1. Study Dosing Regimen

Cohort	Group	Age	Weight at Baseline (kg)	ODV or Placebo Dosing Regimen (mg)[a]
Cohort 1 (N≥106): Children and infants with baseline weight ≥ 3 kg to < 40 kg (Part A) and ≥ 1.5 kg to < 3 kg (Part B)				
1 Part A	1	(If born full term: GA ≥ 37 weeks and CA ≥ 28 days to < 2 yrs), OR (If born preterm: GA < 37 weeks and PMA < 44 weeks and CA < 2 yrs), OR (CA ≥ 2 to < 5 years)	≥ 20 to < 40	291.5 mg twice on Day 1 and 175 mg twice daily on Days 2 to 5
	2		≥ 12 to < 20	175 mg twice on Day 1 and 116.6 mg twice daily on Days 2 to 5
	3		≥ 6 to < 12	116.6 mg twice on Day 1 and 58.3 mg twice daily on Days 2 to 5
	4		≥ 3 to < 6	50 mg twice on Day 1 and 30 mg twice daily on Days 2 to 5
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CA = chronological age; GA = gestational age; ODV = obeldesivir; PMA = postmenstrual age; SRT = safety review team
a Participants receiving only 1 of 2 doses on Day 1 will need to take their last dose on Day 6.
b The SRT will confirm the ODV doses to be evaluated in Cohort 2 and Cohort 1 Part B from the specified dose ranges.

The study treatment period was 5 days with a posttreatment follow-up period of up to 30 days after the last dose of study drug. For the entire duration of the study, participants and investigators remained blinded to the initial treatment regimen.

The timing of efficacy, PK, and safety assessments are presented in Appendix 1 and Appendix 2.

1.3. Sample Size and Power

The target sample size was at least 130 nonhospitalized participants across 2 cohorts with a minimum of 24 participants for Cohort 2.

Within each cohort/weight group, participants were randomized in a 2:1 ratio to ODV or placebo. The sample size was determined based on practical considerations. It was not formally powered. The sample size would have provided a suitable assessment of the descriptive safety, tolerability, PK, and efficacy profile of ODV.

This study was terminated early; hence the number of participants originally planned to be randomized as outlined above was not achieved.

2. TYPE OF PLANNED ANALYSIS

2.1. Interim Analyses

As the study has been terminated early, interim analyses are no longer required.

2.1.1. Dose Confirmation Analysis

As the study has been terminated early, dose confirmation analyses are no longer required.

2.1.2. Data Monitoring Committee Analyses

As the study has been terminated early, data monitoring committee analyses are no longer required.

2.2. Final Analysis

The unblinded final analysis will be performed after all participants enrolled at the time of study termination have completed the study, outstanding data queries have been resolved or adjudicated as unresolvable, and the data have been cleaned and finalized.

2.3. Changes from Protocol-Specified Analyses

This study was terminated early; hence only the analyses outlined in the subsequent sections will be performed.

3. GENERAL CONSIDERATIONS FOR DATA ANALYSES

Analysis results will be presented using descriptive statistics. For categorical variables, the number and percentage of participants in each category will be presented; for continuous variables, the number of participants (n), mean, standard deviation (SD) or standard error (SE), median, first quartile (Q1), third quartile (Q3), minimum, and maximum will be presented.

By-participant listings will be presented for all participants in the All Randomized Analysis Set and sorted by cohort/weight group, participant identifier (ID) number in ascending order, visit date, and time (if applicable), unless otherwise specified. Data collected on log forms, such as AEs, will be presented in chronological order within the participant. The cohort/weight group and treatment group to which participants were randomized will be used in the listings. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

3.1. Analysis Sets

Analysis sets define the participants to be included in an analysis. Analysis sets and their definitions are provided in this section. Participants included in each analysis set will be determined before the study blind is broken for analysis. The analysis set will be identified and included as a subtitle of each table, figure, and listing.

For each analysis set, the number and percentage of participants eligible for inclusion will be summarized by treatment group (overall and within each cohort/weight group) and overall.

A listing of participants excluded from any analysis set will be provided.

3.1.1. All Randomized Analysis Set

The All Randomized Analysis Set includes all participants who were randomized in the study.

3.1.2. Full Analysis Set

The Full Analysis Set (FAS) includes all randomized participants who took at least 1 dose of study drug.

3.1.3. Full Analysis Positive Set

The Full Analysis Positive Set (FAPS) includes participants in the FAS who are RSV positive at baseline by a central laboratory test. RSV positive is defined as RSV positive at baseline as confirmed by RNA viral load RT-qPCR test and/or multiplex BioFire RP2.1 respiratory pathogen panel test in universal transport medium (UTM) sample. Refer to Appendix 4 for the details of FAPS determination. Participants with a missing RSV viral load result in UTM nasal swab sample at baseline will be assumed to be RSV positive. This is the primary analysis set for efficacy analyses.

3.1.4. Safety Analysis Set

The Safety Analysis Set includes all randomized participants who took at least 1 dose of study drug. This is the primary analysis set for safety analyses.

3.1.5. Virology Analysis Set

The Virology Analysis Set includes all randomized participants who took at least 1 dose of study drug and have a baseline RSV viral load greater than or equal to the lower limit of quantitation (LLOQ). This is the primary analysis set for all virology analyses.

Refer to Section 3.7 for the definition of LLOQ.

3.1.6. Pharmacokinetic Analysis Set

The PK Analysis Set includes all randomized participants who took at least 1 dose of study drug and have at least 1 nonmissing result for PK evaluation of GS-441524. This is the primary analysis set for all PK analyses.

3.2. Participant Grouping

For all analyses, participants will be grouped according to the cohort/weight group to which participants were randomized.

For analyses based on the All Randomized Analysis Set, FAS, FAPS, and Virology Analysis Set, participants will be grouped according to the treatment to which they were randomized. For analyses based on the Safety Analysis Set, participants will be grouped according to the actual treatment received. The actual treatment received will differ from the randomized treatment only when their actual treatment differs from randomized treatment for the entire treatment duration.

For the PK Analysis Set, participants will be grouped according to the actual treatment they received.

3.3. Strata and Covariates

Although the randomization is stratified by cohort/weight group, cohort/weight group will not be used as a covariate in any analysis model because the study was terminated early resulting in small sample sizes for the cohort/weight groups.

3.4. Examination of Participant Subgroups

There are no prespecified participant subgroupings for efficacy and safety analyses.

3.5. Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

3.6. Missing Data and Outliers

3.6.1. Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified. Exceptions are presented in this document.

The handling of missing or incomplete dates for AE start is described in Section 7.1.5.2, and for prior and concomitant medications in Section 7.4.

3.6.2. Outliers

Outliers of non-PK data will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. Unless specified otherwise, all data will be included in the data analysis.

3.7. Data Handling Conventions and Transformations

The following conventions will be used for the imputation of date of birth when it is partially missing or not collected:

- If only month and year of birth is collected, then "15" will be imputed as the day of birth
- If only year of birth is collected, then "01 July" will be imputed as the day and month of birth
- If year of birth is missing, then date of birth will not be imputed.

In general, age collected at Day 1 (in years or months) will be used for analyses and presented in listings. If age at Day 1 is not available for a participant, then age derived based on date of birth and the Day 1 visit date will be used instead. If an enrolled participant was not dosed with any study drug, the randomization date will be used instead of the Day 1 visit date. For screen failures, the date the first informed consent was signed will be used for the age derivation. Age required for longitudinal and temporal calculations and analyses (eg, estimates of creatinine clearance, age at start date of AE) will be based on age derived from date of birth and the date of the measurement or event, unless otherwise specified.

Non-PK data (other than viral load data) that are continuous in nature but are less than the LLOQ or above the upper limit of quantitation (LOQ) will be imputed as follows:

- A value that is 1 unit less than the LLOQ at the same precision level of the originally reported value will be used to calculate descriptive statistics if the datum is reported in the form of "< x" (where x is considered the LLOQ. For example, if the values are reported as < 50 and < 5.0, values of 49 and 4.9, respectively, will be used to calculate summary statistics. An exception to this rule is any value reported as < 1 or < 0.1, etc. For values reported as < 1 or < 0.1, a value of 0.9 or 0.09, respectively, will be used to calculate summary statistics.

- A value that is 1 unit above the upper LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "> x" (where x is considered the upper LOQ). Values with decimal points will follow the same logic as above.

- The lower or upper LOQ will be used to calculate descriptive statistics if the datum is reported in the form of "≤ x" or "≥ x" (where x is considered the lower or upper LOQ, respectively).

If methods based on the assumption that the data are normally distributed are not adequate, analyses may be performed on transformed data or nonparametric analysis methods may be used, as appropriate.

The LLOQ of RSV-A and RSV-B viral load were determined to be 1000 copies/mL and 250 copies/mL, respectively. The limit of detection (LOD) of the assay for RSV-A and RSV-B were determined to be 620 copies/mL and 80 copies/mL, respectively. The LLOQ of RNase P was determined to be 2000 Haploid GE/mL. A baseline RSV viral load greater than or equal to the LLOQ refers to either RSV-A ≥ 1000 copies/mL or RSV-B ≥ 250 copies/mL. RSV viral load results that are below LLOQ but have a positive signal will be reported as "target detected" and those that are below lower LOD and negative will be reported as "target not detected". The data will be imputed as follows:

- For RSV-A, a value of 500 copies/mL (half of the LLOQ 1000 copies/mL) will be used to calculate descriptive statistics if the datum is reported as "target detected".

- For RSV-B, a value of 125 copies/mL (half of the LLOQ 250 copies/mL) will be used to calculate descriptive statistics if the datum is reported as "target detected".

- For RSV-A, a value of 310 copies/mL (half of the LOD 620 copies/mL) will be used to calculate descriptive statistics if the datum is reported as "target not detected".

- For RSV-B, a value of 40 copies/mL (half of the LOD 80 copies/mL) will be used to calculate descriptive statistics if the datum is reported as "target not detected".

For participants who are classified as RSV-B only at baseline, RSV-A viral load will not be imputed. For participants who are classified as RSV-A only at baseline, RSV-B viral load will not be imputed.

The lower limit of detection (LLOD) and LLOQ are both 1.52 $\log_{10}$ TCID 50/mL for the infectious viral titer (IVT) assay. The upper limit of detection (ULOD) and upper limit of quantitation (ULOQ) for the IVT assay are 9.04 $\log_{10}$ TCID50/mL and 6.35 $\log_{10}$ TCID50/mL, respectively. The RSV IVT data will be imputed as follows:

- A value of 0.92 $\log_{10}$ TCID50/mL (1/4 of the LLOD 1.52 $\log_{10}$ TCID50/mL, after an inverse log transformation) will be used to calculate descriptive statistics if the datum is reported as "< 1.52 $\log_{10}$ TCID50/mL". The corresponding qualitative result is "Negative".

- A value of 9.05 $\log_{10}$ TCID50/mL (1 unit above the ULOD) will be used to calculate descriptive statistics if the datum is reported as "> 9.04 $\log_{10}$ TCID50/mL". The corresponding qualitative result is "Positive".

- A value of 6.36 $\log_{10}$ TCID50/mL (1 unit above the ULOQ) will be used to calculate descriptive statistics if the datum is reported as "> 6.35 $\log_{10}$ TCID50/mL". The corresponding qualitative result is "Positive".

PK concentration values that are below the limit of quantitation (BLQ) will be presented as "BLQ" in the data listing.

Values that are BLQ will be treated as 0 at predose and postdose time points for summary purposes. The number of samples will be summarized to reflect the actual number of samples assessed at that time point.

At predose, if all concentration values are BLQ, then the mean, and order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as 0 and the rest of the summary statistics (ie, SD and CV) will be missing. If any values are non-BLQ, then the number of samples, order statistics, and all summary statistics will be displayed.

At any given postdose time point, if more than one-third of the participants have a concentration value of BLQ, then only the number of samples and order statistics will be displayed; otherwise, order statistics and summary statistics will be displayed.

The following conventions will be used for the presentation of order statistics for postdose time points:

- If at least 1 participant has a concentration value of BLQ for the time point, the minimum value will be displayed as "BLQ."

- If more than 25% of the participants have a concentration data value of BLQ for a given time point, the minimum and Q1 values will be displayed as "BLQ."

- If more than 50% of the participants have a concentration data value of BLQ for a given time point, the minimum, Q1, and median values will be displayed as "BLQ."

- If more than 75% of the participants have a concentration data value of BLQ for a given time point, the minimum, Q1, median, and Q3 values will be displayed as "BLQ."

- If all participants have concentration data values of BLQ for a given time point, all order statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ."

3.8. Analysis Visit Windows

3.8.1. Definition of Study Day

Study day will be calculated from the first dosing date of study drug and derived as follows:

- For postdose study days: Assessment Date – First Dosing Date + 1

- For days prior to the first dose: Assessment Date – First Dosing Date

Therefore, **Study Day 1** is the day of first dose of study drug administration.

First Dosing Date is defined as the minimum, nonmissing, nonzero dose date of treatment recorded on the Study Drug Administration eCRF.

Last Dose Date is defined as the maximum, nonmissing, nonzero dose date of treatment recorded on the Study Drug Administration eCRF with "Check box if study drug was permanently withdrawn" checked for participants who prematurely discontinued or completed study drug according to the Study Drug Completion eCRF.

Last Study Date is the latest of the study drug start dates and end dates, the in-person or virtual visit dates, the vital sign collection dates, the questionnaire collection dates, the laboratory collection dates, and the death date (if applicable, for participants who died during the study, the death date will be the Last Study Date. For participants who died after completing the study or after prematurely discontinuing the study, the death date will not be considered for the Last Study Date).

Baseline value is defined as the last value obtained on or prior to the first dose date (and time, if available), unless otherwise specified.

3.8.2. Analysis Visit Windows

Participant visits might not occur on protocol-specified days. Therefore, for the purpose of analysis, observations will be assigned to analysis windows.

The analysis windows for body weight and height/length/head circumference are provided in Table 3-1.

Table 3-1. Analysis Visit Windows for Body Weight and Height/Length/Head Circumference

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Day 10	10	2	≥ 10

The analysis windows for vital signs and RSV nasal swab viral load are provided in Table 3-2.

Table 3-2. Analysis Visit Windows for Vital Signs and Nasal Midturbinate Swab Samples

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Day 3	3	2	4*
Day 5	5	4*	7
Day 10	10	8	≥ 10

* If the nominal visit is a scheduled visit and the assessment is done on Day 4 (Study Day = 4), assign to Day 3 or Day 5 analysis window based on the nominal visit label. If the nominal visit is an unscheduled visit or early discontinuation visit on Day 4, assign to Day 3 analysis window.

The analysis windows for clinical laboratory assessments are provided in Table 3-3.

Table 3-3. Analysis Visit Windows for Hematology and Chemistry Laboratory Assessments

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Day 5	5	2	8*
Day 10	10	8*	≥ 10

* If the nominal visit is a scheduled visit and the assessment is done on Day 8 (Study Day = 8), assign to Day 5 or Day 10 analysis window based on the nominal visit label. If the nominal visit is an unscheduled visit or early discontinuation visit on Day 8, assign to Day 5 analysis window.

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The analysis windows for palatability and acceptability are provided in Table 3-4.

Table 3-4. Analysis Visit Windows for Palatability and Acceptability Assessments

Visit	Study Day	Visit Window Study Day	
		Lower Limit	Upper Limit
Baseline	1	(none)	1
Day 5	5	2	≥5

3.8.3. Selection of Data in the Event of Multiple Records in an Analysis Visit Window

Depending on the statistical analysis method, single values may be required for each analysis window. For example, change from baseline by visit usually requires a single value, whereas a time-to-event analysis would not require 1 value per analysis window.

If multiple valid, nonmissing measurements exist in an analysis window, records will be chosen based on the following rules if a single value is needed:

- For baseline questionnaire data, the last nonmissing value on or prior to the first dosing date of study drug will be selected. If there are multiple records on or prior to the first dosing date, the record prior to and closest to the first dosing date and time will be used if available; otherwise, the record after and closest to the first dose date and time will be used.

- For baseline data other than questionnaire, the last nonmissing value on or prior to the first dosing date of study drug will be selected, unless specified differently. If there are multiple records on the same day, the baseline value will be selected as follows:

  — For continuous data:

    ■ For RSV viral load and infectious viral titer data, if there is more than 1 record on the selected day, the latest value will be selected. Within each of viral load sample category types, if there are multiple records with the same time or no time recorded on the same day, the geometric mean value will be taken.

    ■ For other continuous data, the baseline value will be the average of the measurements.

- For categorical data:
  - For RSV positivity based on RT-qPCR, Multiplex PCR, the worst severity (ie, a positive PCR result) will be selected.
  - For other categorical data, the baseline value will be the measurement with the lowest severity.

- For postbaseline values:
  - The record closest to the nominal day for that visit will be selected.
  - If there are 2 records that are equidistant from the nominal day, the later record will be selected.
  - If there is more than 1 record on the selected day, values will be selected for analysis as follows:
    - For RSV viral load and infectious viral titer, if there is more than 1 record on the selected day, the latest value will be selected. If there are multiple records with the same time or no time recorded on the same day, the geometric mean value will be taken.
    - For questionnaire data to be summarized, if there is more than 1 record on the selected day, the latest value will be selected.
    - For other parameters, if there is more than 1 record on the selected day, the average will be taken for continuous data and the worse severity will be taken for categorical data, unless otherwise specified.

4. PARTICIPANT DISPOSITION

4.1. Participant Enrollment and Disposition

Key study dates (ie, first participant screened, first participant randomized, last participant randomized, and last participant last visit for the clinical study report) will be provided.

A summary of participant enrollment will be provided by treatment group (overall and within each cohort/weight group) for each investigator within a country, and overall using the All Randomized Analysis Set. The summary will present the number and percentage of participants enrolled. For each column, the denominator for the percentage calculation will be the total number of participants analyzed for that column.

A summary of participant disposition will be provided by treatment group (overall and within each cohort/weight group) and overall. This summary will present the number of participants screened, the number of participants who met all eligibility criteria but were not randomized with reasons for participants not randomized, the number of participants randomized, and the number of participants in each of the categories listed below:

- Safety Analysis Set
- Full Analysis Set
- Full Analysis Positive Set
- PK Analysis Set
- Virology Analysis Set
- Completed study drug
- Did not complete study drug with reasons for premature discontinuation of study drug
- Completed study
- Did not complete the study with reasons for premature discontinuation of study

For the status of study drug and study completion and reasons for premature discontinuation, the number and percentage of participants in each category will be provided. The denominator for the percentage calculation will be the total number of participants in the Safety Analysis Set corresponding to that column.

The following by-participant listings will be provided by participant ID number in ascending order to support the above summary tables:

- Participant disposition, including cohort/weight group, treatment group, date of randomization, first dose date, last dose date, end of study date, study drug discontinuation, study discontinuation, and reasons for study drug or study discontinuation.

- Reasons for screen failure (will be provided by screening ID number in ascending order)

4.2. Extent of Study Drug Exposure and Adherence

Extent of exposure to study drug will be examined by assessing the total duration of exposure to study drug and the level of adherence relative to the study drug regimen specified in the protocol.

4.2.1. Duration of Exposure to Study Drug

Total duration of exposure to study drug will be defined as last dosing date minus first dosing date plus 1, regardless of any temporary interruptions in study drug administration, and will be expressed in days. A by-participant listing of study drug administration and drug accountability will be provided by participant ID number (in ascending order) and visit (or timepoint if applicable) (in chronological order).

4.3. Protocol Deviations

Protocol deviations occurring after participants entered the study are documented during routine monitoring. A by-participant listing will be provided for those participants with protocol deviations, including a column specifying whether the protocol deviation is important.

5. BASELINE CHARACTERISTICS

5.1. Demographics and Baseline Characteristics

Participant demographic variables (age, sex at birth, race, and ethnicity) and baseline characteristics (body weight [in kg], body weight-age Z-scores, height/length [in cm], height-age Z-scores, body mass index [BMI; in kg/m^2], BMI-age Z-scores, BMI-age percentile, head circumference [in cm]) will be summarized by treatment group (overall and within each cohort/weight group) and overall using descriptive statistics for continuous variables and using number and percentage of participants for categorical variables. The summary of demographic data will be provided for the Safety Analysis Set. Missing values including not permitted will not be included in the denominator when calculating percentages.

A by-participant demographic listing, including the informed consent date, will be provided by participant ID number in ascending order. Note: If information on GA and postmenstrual age (PMA) for participants with GA < 37 weeks and chronological age (CA) < 2 years or length and head circumference for participants < 2 years of age at screening has been collected, this information will be listed. Details on calculating Z-score and percentiles for weight, height/length and BMI are available in Appendix 4.

5.2. Other Baseline Characteristics

Other baseline characteristics include:

- Duration of RSV sign or symptom prior to the first dose of study drug (days)
  - Defined as: First Dosing Date – Onset Date of First/Earliest RSV Sign or Symptom
- Duration from first positive RSV diagnostic test to first dosing date (days)
  - Defined as: First Dosing Date – Date of RSV Diagnosis
- Risk factors for severe RSV disease: (a) None; (b) Yes subdivided into: (i) Aged ≤ 6 months of age; (ii) Aged < 1 year of age and born prematurely (GA < 37 weeks); (iii) Congenital heart disease; (iv) Bronchopulmonary dysplasia; (v) Down syndrome; (vi) Neuromuscular conditions including cerebral palsy
  - Note: Participants may have more than 1 risk factor for severe RSV disease.
- Total number of risk factors for severe RSV disease
- CCI [redacted]
- Severity of each targeted RSV symptom at baseline

- Baseline creatinine
- Baseline estimated glomerular filtration rate using Beside Schwartz formula ($eGFR_{Bedside\ Schwartz}$) (mL/min/1.73 m^2)
- Baseline alanine aminotransferase (ALT) (U/L)
- RSV subtype at baseline: (a) RSV-A only; (b) RSV-B only; (c) RSV-A/B Coinfection; (d) Not Determined
- Baseline RSV viral load in UTM Swabs: combined RSV, RSV-A, and RSV-B (as a continuous variable)
- Baseline RSV infectious viral titer (as a continuous variable)

A by-participant listing of other baseline characteristics will be provided by participant ID number in ascending order.

5.3. Medical History

Medical history will be collected at screening for general conditions (ie, conditions not specific to the disease being studied). Medical history will be coded using the current Medical Dictionary for Regulatory Activities (MedDRA) dictionary.

A by-participant listing of medical history will be provided by participant ID number in ascending order.

6. EFFICACY ANALYSES

6.1. Primary Efficacy Endpoint

The FAPS will be used for the primary efficacy endpoint analysis.

6.1.1. Definition of the Primary Efficacy Endpoint

The primary efficacy endpoint is time to alleviation of targeted RSV symptoms by Day 28.

For nonhospitalized participants, alleviation of targeted RSV symptoms is defined as:

[redacted]

The date and time of the first day of the 2 daily consecutive assessments will be considered as the date and time of alleviation of targeted RSV symptoms. [redacted]. The date and time stamps at which caregivers complete the questionnaire are captured in an electronic diary and the later of the OS assessment time and the DS assessment time will be considered as the assessment time for that day.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted].

6.1.2. Primary Analysis of the Primary Efficacy Endpoint

The primary estimand for the primary efficacy endpoint is outlined in the following table.

Table 6-1. Primary Estimand for Primary Efficacy Endpoint

Attribute	Details
Target population	Study population as defined by protocol eligibility criteria
Treatment condition(s)	ODV and placebo, regardless of treatment discontinuation/modification, RSV-related hospitalization, or RSV-related MAVs
Variable	Time (days) to alleviation of targeted RSV symptoms by Day 28 in the absence of rescue medication and all-cause death
Handling of ICEs	The following scenarios if they occur prior to alleviation of targeted RSV symptoms by Day 28 will be considered: • Treatment discontinuation/modification: treatment policy (included as part of the treatment condition(s) attribute) • Use of rescue medication: composite strategy (included as part of the variable attribute). Note: details on the rescue medications are presented in Appendix 4. • All-cause death: composite strategy (included as part of the variable attribute) • RSV-related hospitalization: treatment policy (included as part of the treatment condition(s) attribute) • RSV-related MAVs: treatment policy (included as part of the treatment condition(s) attribute)
Population-level summary	Difference in median variable (as defined in the variable attribute) between ODV and placebo

ICE = intercurrent events; MAV = medically attended visit; ODV = obeldesivir; RSV = respiratory syncytial virus

For participants with targeted RSV symptom alleviation by Day 28 (ie, event), the time to alleviation of targeted RSV symptoms by Day 28 is calculated as the symptom alleviation date/time minus the first dose date/time (expressed as days with 8 decimal places). In the analysis output, 1 decimal place in days will be used for display purposes.

In case, a participant:

- Completes the study without alleviation of targeted RSV symptoms (ie, censored)
- Prematurely discontinues from the study prior to alleviation of targeted RSV symptoms (due to AE, lack of efficacy, investigator's discretion, noncompliance with study drug, protocol violation, participant decision, lost to follow-up) (ie, censored)

The time to alleviation of targeted RSV symptoms will be calculated as the last date and time on which the symptom alleviation is assessed or 23:59:00 on Day 27, whichever occurs first, minus the first dose date and time.

Treatment discontinuation/modification, RSV-related hospitalization, and/or RSV-related MAVs will be ignored (treatment policy).

If a participant takes rescue medication or dies prior to alleviation of targeted RSV symptoms (ie, composite strategy), alleviation of targeted RSV symptoms will not have been achieved. The participant will be censored at the last date and time on which symptom alleviation is assessed prior to the start of rescue medication or death.

CCI [redacted]

[redacted]

Time to alleviation of targeted RSV symptoms by Day 28 will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, mininum and maximum) by censoring status (event or censored) for each treatment group.

6.2. Secondary Efficacy Endpoints

6.2.1. Definition of the Secondary Efficacy Endpoints

6.2.1.1. Time to Sustained Alleviation of Targeted RSV Symptoms by Day 28

For nonhospitalized participants, sustained alleviation of targeted RSV symptoms is defined similarly to alleviation of targeted RSV symptoms (see Section 6.1.1) but for 3 daily consecutive assessments (ie, 48-hour period).

CCI [redacted]

In case, a participant:

- Completes the study without sustained alleviation of targeted RSV symptoms (ie, censored)
- Prematurely discontinues from the study prior to sustained alleviation of targeted RSV symptoms (due to AE, lack of efficacy, investigator's discretion, noncompliance with study drug, protocol violation, participant decision, lost to follow-up) (ie, censored)

The time to sustained alleviation of targeted RSV symptoms will be calculated as the last date and time on which the sustained alleviation is assessed or 23:59:00 on Day 26, whichever occurs first, minus the first dose date and time.

6.2.1.2. Time to Resolution of Targeted RSV Symptoms by Day 28

For nonhospitalized participants, resolution of targeted RSV symptoms is defined as:

CCI

CCI

The date and time of the first day of the 2 daily consecutive assessments will be considered as the date and time of resolution of targeted RSV symptoms.

In case, a participant:

- Completes the study without resolution of targeted RSV symptoms (ie, censored)
- Prematurely discontinues from the study prior to resolution of targeted RSV symptoms (due to AE, lack of efficacy, investigator's discretion, noncompliance with study drug, protocol violation, participant decision, lost to follow-up) (ie, censored)

CCI

Targeted RSV symptoms are defined in Section 6.1.1.

6.2.2. Secondary Analyses

The primary estimands for the secondary efficacy endpoint are outlined in the following table.

Table 6-2. Primary Estimand for Secondary Efficacy Endpoints

Attribute	Details		
Endpoint	Change from baseline in RSV nasal swab viral load at Day 5	Time to sustained alleviation of targeted RSV symptoms by Day 28	Time to resolution of targeted RSV symptoms by Day 28
Target population	Study population as defined by protocol eligibility criteria		
Treatment condition(s)	ODV and placebo, regardless of treatment discontinuation/modification, RSV-related hospitalization, or RSV-related MAVs		
Variable	Change from baseline in RSV nasal swab viral load at Day 5 in the absence of rescue medication and all-cause death	Time (days) to sustained alleviation of targeted RSV symptoms by Day 28 in the absence of rescue medication and all-cause death	Time (days) to resolution of targeted RSV symptoms by Day 28 in the absence of rescue medication and all-cause death
Handling of ICEs	• Treatment discontinuation/modification: treatment policy (included as part of the treatment condition(s) attribute) • Use of rescue medication: composite strategy (included as part of the variable attribute) • All-cause death: composite strategy (included as part of the variable attribute) • RSV-related hospitalization: treatment policy (included as part of the treatment condition(s) attribute) • RSV-related MAVs: treatment policy (included as part of the treatment condition(s) attribute)		
Population-level summary	Difference in least square means variable (as defined in the variable attribute) between ODV and placebo	Difference in median variable (as defined in the variable attribute) between ODV and placebo	

ICE = intercurrent events; MAV = medically attended visit; ODV = obeldesivir; RSV = respiratory syncytial virus

Similar analyses as outlined in Section 6.1.2 will be performed on time to sustained alleviation and time to resolution of targeted RSV symptoms by Day 28 using the FAPS.

Time to sustained alleviation and time to resolution of targeted RSV symptoms by Day 28 will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, mininum and maximum) by censoring status (event or censored) for each treatment group.

Scores of targeted RSV symptoms will be provided in a by-participant listing sorted by participant ID number and assessment date. The time to alleviation, sustained alleviation and resolution of targeted RSV symptoms will be provided in the listing.

CCI [redacted].

Analysis of virology data will be conducted in the Virology Analysis Set. The change from baseline in RSV nasal swab viral load at each visit will be summarized by treatment group using descriptive statistics. Any RSV viral load samples collected on or after the day when participants are receiving rescue medications (except for Danirixin, Chlorpheniramine maleate and Asapiprant) will be excluded from the viral load analysis.

Viral load results will be provided in a by-participant listing sorted by participant ID number and visit.

6.3. Changes From Protocol-Specified Efficacy Analyses

This study was terminated early. Due to the limited number of participants enrolled in the study at the time of study termination, efficacy endpoints will be summarized by treatment group using descriptive statistics only. No inferential analyses will be performed.

7. SAFETY ANALYSES

Analysis of safety data will be conducted on the Safety Analysis Set, unless otherwise specified in the following sections. The treatment-emergent (TE) period is defined as the time period from the first dose date of study treatment up to and including 30 days after the last dose of study treatment.

All safety data during the TE period will be summarized by treatment group as defined in Section 3.2. Data for the pretreatment and treatment-free follow-up periods will be included in data listings.

7.1. Adverse Events and Deaths

7.1.1. Adverse Event Dictionary

Clinical and laboratory adverse events (AEs) will be coded using the current version (28.1) of MedDRA. System organ class (SOC), high-level group term (HLGT), high-level term (HLT), preferred term (PT), and lowest-level term (LLT) will be provided in the AE dataset.

7.1.2. Adverse Event Severity

The severity of AEs will be graded using the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 dated July 2017. For each episode, the highest grade attained should be reported as defined in the grading scale.

Adverse events are graded by the investigator as Grade 1, 2, 3, 4, or 5 according to toxicity criteria specified in the protocol. The severity grade of events for which the investigator did not record severity will be categorized as “missing” for tabular summaries and data listings. The missing category will be listed last in summary presentation.

7.1.3. Relationship of Adverse Events to Study Drug

Related AEs are those for which the investigator selected “Related” on the AE eCRF to the question of “Related to Study Treatment”. Relatedness will always default to the investigator’s choice, not that of the medical monitor. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-participant data listings will show the relationship as missing.

7.1.4. Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol. SAEs captured and stored in the clinical database will be reconciled with the SAE database from the Gilead Patient Safety Department before data finalization.

7.1.5. Treatment-Emergent Adverse Events

7.1.5.1. Definition of Treatment-Emergent Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as:

- Any AEs that start during the TE period (Section 7)

7.1.5.2. Incomplete Dates

If the start date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of start determine whether an AE is TE. The event is considered TE if both of the following 2 criteria are met:

- The AE start date is the same as or after the month and year (or year) of the first dosing date of study drug, and
- The AE start date is the same as or before the month and year (or year) of the last day of the TE period

An AE with completely missing start and stop dates, or with the start date missing and a stop date later than the first dosing date of study drug, will be considered to be TE. In addition, an AE with the start date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered TE.

7.1.6. Summaries of Adverse Events and Deaths

Treatment-emergent AEs will be summarized by treatment group (overall and within each cohort/weight group) and overall based on the Safety Analysis Set.

A brief, high-level summary of the number and percentage of participants who experienced at least 1 TEAE in the categories described below will be provided.

- TEAE
- TEAEs by Day 28
- TEAEs with Grade 3 or higher
- TE treatment-related AEs

- TE treatment-related AEs with Grade 3 or higher
- TE SAEs
- TE treatment-related SAEs
- TEAEs leading to premature discontinuation of study drug
- TEAEs leading to premature discontinuation of study
- TE AEs leading to death (ie, Grade 5 AEs)

The number and percentage of participants who experienced at least 1 TEAE will be provided and summarized by SOC, HLT (if applicable), and PT for the following categories.

- TEAEs
- TEAEs by Day 28
- TEAEs with Grade 3 or higher
- TE SAEs

Multiple events will be counted only once per participant in each summary. Adverse events will be summarized and listed first in alphabetic order of SOC (and HLT within each SOC if applicable), and then by PT in descending order of total frequency within each SOC.

In addition to the above summary tables, all TEAEs, TEAEs by Day 28, TEAEs with Grade 3 or higher, and TE SAEs will be summarized by PT only, in descending order of total frequency.

In addition, data listings will be provided for the following:

- All AEs, indicating whether the event is TE
- All AEs with severity of Grade 3 or higher
- All AEs leading to premature discontinuation of study drug
- All AEs leading to premature discontinuation of study
- All SAEs
- All Deaths
- All SAEs leading to death (i.e., outcome of death)

7.2. Laboratory Evaluations

Laboratory data collected during the study will be analyzed using both quantitative and qualitative methods. The analysis will be based on values reported in conventional units. When values are below the LOQ, they will be listed as such, and the closest imputed value will be used for the purpose of calculating summary statistics as specified in Section 3.7.

A by-participant listing for laboratory test results will be provided by participant ID number and time point in chronological order for hematology and serum chemistry separately. Values falling outside of the relevant reference range and/or having a severity grade of 1 or higher will be flagged in the data listings, as appropriate.

7.2.1. Graded Laboratory Values

The DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 dated July 2017 will be used to assign toxicity grades (0 to 4) to laboratory results for analysis. Grade 0 includes all values that do not meet the criteria for an abnormality of at least Grade 1. For laboratory tests with criteria for both increased and decreased levels, analyses for each direction (i.e., increased, decreased) will be presented separately.

7.2.1.1. Treatment-Emergent Laboratory Abnormalities

Treatment-emergent laboratory abnormalities (TELAs) are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point during the TE period defined at the beginning of Section 7. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered TE.

7.2.1.2. Summaries of Laboratory Abnormalities

Laboratory data that are categorical will be summarized using the number and percentage of participants in the study with the given response at baseline and each scheduled postbaseline time point.

The following summaries (number and percentage of participants) for TELAs will be provided by lab test, treatment group (overall and within each cohort/weight group) and overall; participants will be categorized according to the most severe postbaseline abnormality grade for a given lab test:

- Graded TELAs
- Grade 3 or 4 TELAs
- Grade 3 or 4 TELAs by Day 28

For all summaries of laboratory abnormalities, the denominator is the number of participants with nonmissing postbaseline values during the TE period defined at the beginning of Section 7.

By-participant listings of graded TELAs and Grade 3 or 4 TELAs will be provided by participant ID number and visit in chronological order. This listing will include all test results that were collected throughout the study for the lab test of interest, with all applicable severity grades (or abnormal flags, if applicable) displayed.

7.2.2. Liver-related Laboratory Evaluations

Liver-related abnormalities after initial study drug dosing are defined as the following laboratory test values for postbaseline measurements:

- Aspartate aminotransferase (AST): (a) > 3 times of the upper limit of reference range (ULN); (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Alanine aminotransferase (ALT): (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- AST or ALT: (a) > 3 x ULN; (b) > 5 x ULN; (c) > 10 x ULN; (d) > 20 x ULN
- Total bilirubin: (a) > 1 x ULN; (b) > 2 x ULN
- Alkaline phosphatase (ALP) > 1.5 x ULN
- AST or ALT > 3 x ULN and total bilirubin: (a) > 1.5 x ULN; (b) > 2 x ULN
- AST or ALT > 3 x ULN, ALP < 2 x ULN, and associated with TBL > 2 x ULN (Hy's Law)

A listing of participants who met at least 1 of the above criteria will be provided.

7.3. Body Weight, Height, and Vital Signs

An age- and sex-specific Z-score will be derived for each weight, height/length, and BMI measurement. For participants ≥ 2 years, this will be based on the Centers for Disease Control and Prevention (CDC) year 2000 growth charts for those without severe obesity and CDC's year 2022 extended BMI-for-Age growth charts for those with severe obesity. The World Health Organization (WHO) growth charts will be used for participants < 2 years.

A by-participant listing of vital signs will be provided by participant ID number and time point in chronological order. Body weight, body weight Z-scores, height/length, height/length Z-scores, BMI, BMI Z-scores, and head circumference will be included in the vital signs listing, if space permits. If not, they will be provided separately.

7.4. Prior and Concomitant Medications

Medications collected at screening and during the study will be coded using the current version of the World Health Organization (WHO) Drug dictionary.

Prior medications are defined as any medications taken before a participant took the first study drug.

Any medication with a start date prior to the first dosing date of study drug is a prior medication regardless of when the stop date is. If a partial start date is entered the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be considered as a prior medication, unless otherwise specified.

Concomitant medications are defined as medications taken while a participant took study drug. All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-participant listing sorted by participant ID number and administration date in chronological order.

7.5. Palatability and Acceptability Assessments

Palatability and acceptability assessments will be summarized by treatment group (overall and within each cohort/weight group) and overall for each visit using frequency count and percentage.

Palatability and acceptability assessments will be provided in a by-participant listing sorted by participant ID number and visit.

7.6. Other Safety Measures

Hospitalization and MAVs will be provided in a by-participant listing sorted by participant ID number and visit.

7.7. Changes From Protocol-Specified Safety Analyses

This study was terminated early; due to limited data, continuous safety data, including laboratory test data, will be provided in by-participant listings only.

8. PHARMACOKINETIC (PK) ANALYSES

8.1. PK Sample Collection

PK sample collection schedule is in Appendix 2.

8.2. PK Analyses

Individual participant concentration data for ODV metabolite, GS-441524 will be listed and summarized using descriptive statistics by cohort/weight group. Summary statistics (number of participants, mean, SD, coefficient of variation [%CV], median, min, max, Q1, and Q3) will be presented for individual participant concentration data by time point.

Individual concentration data listings and summaries will include all participants with concentration data. The sample size for each time point will be based on the number of participants with nonmissing concentration data at that time point. The number of participants with BLQ concentration, as well as an indicator if more than one-third of the participants are BLQ will be presented for each time point. For summary statistics, BLQ values will be treated as zero at predose and postdose time points. If more than one-third of the values at a postdose time point are BLQ then the mean and SD will not be presented at that time point. Concentration values will be presented as received from the bioanalytical lab and summary statistics will be presented to three significant digits.

The following table will be provided for the analyte of interest by cohort/weight group:

- Individual participant concentration data and summary statistics

The following listing will be provided:

- PK sampling details by participant, including procedures, differences in scheduled and actual draw times, and sample age.

8.3. Changes From Protocol-Specified PK Analyses

Due to the very limited number of participants and sparse PK samples collected in the study, PK parameters are not estimated in this study and only PK concentration data will be summarized.

9. SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA.

10. SAP REVISION

Revision Date (DD MMM YYYY)	Section	Summary of Revision	Reason for Revision

11. APPENDICES

Appendix 1. Study Procedures Table

	Screening[a,b]	Baseline[a]					EOS	ET
Study Day		**Day 1**	**Day 3[c]**	**Day 5**	**Day 10**	**Day 21**	**Day 28**	—
Visit Window	—	—	—	**± 1 d**	**± 2 d**	**± 2 d**	**−4 d/+7 d**	—
Type of Visit	**In Person[d]**					**Virtual[e]**		**In Person[d]**
Assent/caregiver consent	X							
Medical history[f]	X							
Demographics	X							
Documentation of RSV infection[b]	X							
Documentation of SARS-CoV-2 and influenza A/B test negativity[b]	X							
Inclusion/exclusion criteria	X	X						
Complete physical examination[g]	X				X			X
Symptom-directed physical examination[g]		X	X	X				
Body weight	X	X			X			X
Height/length/head circumference[h]	X				X			X
GA and PMA if GA is < 37 weeks for children < 2 years	X							
Vital signs[i]	X	X	X	X	X			X
Hematology, chemistry	X			X	X			X
Neonatal bilirubin panel for all participants < 14 days of age and any neonate as defined in Cohort 2 presenting with jaundice	X							
Nasal midturbinate swab samples[j]		X	X	X	X			X

	Screening[a,b]	Baseline[a]					EOS	ET
Study Day		**Day 1**	**Day 3[c]**	**Day 5**	**Day 10**	**Day 21**	**Day 28**	**—**
Visit Window	**—**	**—**	**—**	**± 1 d**	**± 2 d**	**± 2 d**	**−4 d/+7 d**	**—**
Type of Visit	**In Person[d]**					**Virtual[e]**		**In Person[d]**
GRCD[k]		By caregiver–from Days 1 through 28 or ET inclusive						
CGI-S[l]		By caregiver–on Days 1, 3, 5, 10, 28 or ET						
CGI-C[l]		By caregiver–on Days 3, 5, 10, 28 or ET						
HCPGI-S[m]		X	X	X	X			X
WPAI-RSV[n]		By caregiver–on Days 1, 10, 28 or ET						
HRQOL questionnaires[o]		By caregiver–on Days 1, 5, 10, 28 or ET						
PK sample		Refer to Appendix 2						
Randomization		X						
Study drug dispensation		X						
Study drug administration[p]		Days 1 through 5 inclusive						
Study drug return[q]				X				
Concomitant medications	X	X	X	X	X	X	X	X
MAV/hospitalization/ICU information[r]	X	X	X	X	X	X	X	X
Oxygen supplementation requirements, if hospitalized	X	X	X	X	X	X	X	X
Feeding support information, if hospitalized	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X
Acceptability and palatability assessment		X		X				

CGI-C = Caregiver Global Impression of Change; CGI-S = Caregiver Global Impression of Severity; d = day; EOS = end of study; EQ-5D-5L = EuroQol (5 dimensions, 5 levels); EQ-5D-Y-3L = EuroQol-5 Dimension–child specific (3 levels); ET = early termination; GA = gestational age; GRCD = Gilead RSV Caregiver Diary; HCPGI-S = Health Care Professional Global Impression of Severity; HRQoL = health-related quality of life; ICU = intensive care unit; MAP = mean arterial pressure; MAV = medically attended visit; ODV = obeldesivir; PK = pharmacokinetic(s); PMA = postmenstrual age; RSV = respiratory syncytial virus; qRT-PCR = quantitative reverse transcriptase-quantitative polymerase chain reaction; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; WPAI = Work Productivity and Activity Impairment

a Screening window is within 48 hours of the Day 1 visit. Day 1 visit may occur on the same day as screening. If the screening and Day 1 visits are the same day, do not repeat Day 1 assessments.
b Participants anticipated to be eligible for the study and without documented RSV infection ≤ 3 days prior to randomization, and negative influenza A/B, and SARS-CoV-2 testing ≤ 7 days prior to randomization will be consented for RSV, Influenza A/B, and SARS-CoV-2 testing. Participants who are RSV positive and negative for influenza A/B, and SARS-CoV-2 will be approached to consent for entry into the study.
c Day 3 visit is only required if PK samples cannot be collected on Day 5, otherwise it is an optional visit.
d In person is defined as a visit at a medical facility or elsewhere by a health care professional (where permitted).
e Virtual visit is defined as an interaction with a health care professional using telephone or online-based interaction (eg, telehealth, webcast, video conferencing).
f Medical history will include disease-specific history (including the date of first RSV symptom), disease-related events (including RSV symptoms), available disease treatment history (including maternal RSV vaccine or prophylactic treatment for participants), allergies, and medications taken within 30 days of the screening visit.
g A complete physical examination includes source documentation of general appearance and the following body systems: head, neck, and thyroid; eyes, ears, nose, throat, mouth, and tongue; chest (excluding breasts); respiratory; cardiovascular; lymph nodes, abdomen; skin, hair, nails; musculoskeletal; and neurological. Urogenital and reproductive examination should only be completed if clinically indicated. A physical examination is only conducted if a qualified health care professional is available.
h Record length and head circumference for participants < 2 years of age at screening.
i Vital signs include heart rate, body temperature, blood pressure (MAP if available, systolic and diastolic), respiratory rate, and oxygen saturation and will be recorded after the participant has been resting for ≥ 5 minutes.
j The nasal midturbinate swab sample will be used for RSV viral load by qRT-PCR, potential infectious viral titer assessment, potential resistance testing, and respiratory coinfection assessment (Study Protocol Section 6.3.10.1).
k The caregiver symptom assessment will be completed on stipulated days via the GRCD (Study Protocol Appendix 11.5.1), as outlined in Study Protocol Section 6.3.11.1.
l The caregiver global impression of severity and change will be completed on stipulated days via the CGI-S and CGI-C questionnaires, respectively. For days when ODV is administered, the questionnaire should be filled out before study drug administration.
m The health care professional global impression of severity will be completed on in-person visit days via the HCPGI-S questionnaire. The HCPGI-S questionnaire could be completed by a physician or other qualified health care professional. For days when ODV is administered, the questionnaire should be filled out before study drug administration.
n The impact on caregivers on work/education/volunteering will be evaluated on stipulated days via the WPAI-RSV questionnaire. For days when ODV is administered, the questionnaire should be filled out before study drug administration.
o HRQoL will be completed on stipulated days via EQ-5D-Y-3L (for pediatric participants ≥ 4 years of age at screening, to be completed by the caregiver-proxy reported) and EQ-5D-5L (for caregiver, to be completed by caregiver) questionnaires. The EQ-5D-Y-3L assessment will not be required for participants < 4 years of age at screening. For days when ODV is administered, the questionnaire should be filled out before study drug administration.
p Study drug will be administered twice daily, and administration times will be recorded by investigational site personnel or by the caregiver via a diary. Participants receiving only 1 of 2 doses on Day 1 will need to take their last dose on Day 6. Depending on site visit time, participants will be required to withhold their morning or evening dose prior to arriving to the site on Day 5 (or Day 3, if PK samples are collected on Day 3), as the dose will be administered at the site.
q Study drug bottle should be returned by the participant on Day 5, if the participant has already completed both doses of study drug on that day. If the participant has study drug at the end of the Day 5 visit, the participant may return the study drug bottle during the subsequent in-person visit.
r Medically attended visit information includes any interactions with health care professionals other than study staff or designees including hospitalization; in-person emergency, urgent, or primary care visits; ICU admission; or any other in-person visit attended by the participant and a health care professional.

Appendix 2. PK Sample Collection Schedule

Cohort 1–Part A (Full Sampling Scheme)
N = at least the first 24 participants with weight ≥ 6 kg at baseline
Day 1: 15 minutes (± 3 minutes), 45 minutes (± 9 minutes), and 2 hours (± 24 minutes) postdose
Day 5 (± 1 day) (**or** Day 3): predose, and at 2 hour 30 minutes (± 30 minutes) and 3 hour 30 minutes (± 40 minutes) postdose
Cohort 1–Part A (Reduced Sampling Scheme)
N = rest of the participants in Cohort 1 Part A
Day 5 (± 1 day) (**or** Day 3): predose and at 45 minutes (± 9 minutes), and 1 hour 45 minutes (± 21 minutes) postdose
Cohort 1–Part B
Participants with ≥ 1.5 to < 3 kg weight at baseline
Day 1: 45 minutes (± 9 minutes) postdose **OR** Day 5 (± 1 day) (**or** Day 3): 2 hours (± 24 minutes) postdose
Day 5 (± 1 day) (**or** Day 3): predose (< 5 minutes)
Cohort 2
Participants with weight at baseline ≥ 3 to < 6 kg
Day 1: 45 minutes (± 9 minutes) postdose (optional sample at 15 minutes (± 3 minutes) postdose)
Day 5 (± 1 day) (**or** Day 3): predose and at 2 hour 30 minutes postdose (± 30 minutes)
Participants with weight ≥ 1.5 to < 3 kg at baseline
Day 1: 0.75 hour (± 9 minutes) postdose **OR** Day 5 (± 1 day) (**or** Day 3): 2 hours (± 24 minutes) postdose
Day 5 (± 1 day) (**or** Day 3): predose (< 5 minutes)
A single PK sample should be collected on Day 5 (±1 day) for all participants who discontinue study drug earlier than the last scheduled dose. **A single PK sample should be collected at ET visit for all participants who discontinue study earlier than Day 10.**

ET = early termination; PK = pharmacokinetic(s)
The PK samples must be collected relative to the study drug administered in clinic.
If PK samples cannot be collected on Day 5 (± 1 day), then they should be collected on Day 3; in any case, PK samples should not be collected at both Day 3 and Day 5 visits.
Only if 1 dose was administered in the evening of Day 1, PK samples can be collected on Day 6 relative to the study drug administered in clinic

Appendix 3. Laboratory Values

Calcium Corrected for Albumin

Calcium corrected for albumin will be calculated for the study. The following formula will be used when both serum calcium and albumin results for a given blood drawn are available and serum albumin value is < 4.0 g/dL.

Calcium corrected for albumin (mg/dL) = serum calcium (mg/dL) + 0.8 × (4.0 – albumin (g/dL))

Toxicity grading for calcium will be applied based on the corrected values.

Estimated Glomerular Filtration Rate

The following formulae will be used to calculate $eGFR_{Bedside\ Schwartz}$:

$eGFR_{Bedside\ Schwartz}$ (mL/min/1.73 m^2) = [0.413 × height (cm)] / SCr (mg/dL),

where SCr is standardized serum creatinine.

Appendix 4. Programming Specifications

1) Calculation of age-specified Z-score and percentile for weight, height/length and BMI:

   a) Participants < 24 months: Z-score and percentile will be computed using WHO SAS

      package: www.who.int/toolkits/child-growth-standards/software

   b) Participants ≥ 2 years to < 20 years: Z-score and percentile will be computed based on CDC:

      www.cdc.gov/nccdphp/dnpao/growthcharts/resources/sas.htm

2) Guidance for consideration of RSV positivity on a participant-level, for determination of the FAPS is included below.

   a) As a primary method, RSV RNA Viral Load in UTM samples will be used to inform RSV status for FAPS determination, per the table below.

      i) If RSV RNA Viral Load in UTM samples result is missing, RSV-positivity will be assumed.

      ii) If RSV RNA Viral Load in UTM samples result is negative, Biofire result will be used as a secondary method to include participants with false-negative UTM Viral Load result.

FAPS (+/-) Determination		UTM Viral Load Result			
		Positive	**Negative**	**Invalid RSV Result due to poor sample quality (RnaseP = TND)**	**Missing**
Biofire Result	**Positive**	*FAPS(+)*	*FAPS(+)*	*FAPS(+)*	*FAPS(+)*
	Negative	*FAPS(+)*	FAPS(-)	*FAPS(+)*	*FAPS(+)*
	Assay Failure (NRR)	*FAPS(+)*	FAPS(-)	*FAPS(+)*	*FAPS(+)*
	Missing	*FAPS(+)*	FAPS(-)	*FAPS(+)*	*FAPS(+)*

   b) Participants who are RSV positive include those having viral load detected by qRT-PCR, even if the result is below LLOQ, as well as any participants who have RSV detected by the BIOFIRE multiplex assay.

   c) RSV positivity is determined by either RT-qPCR or BioFire assay in UTM. Participant is defined as RSV positive at baseline when viral load result in UTM is missing. If RSV viral load is negative at baseline in UTM, along with a positive BioFire result, then the participant is RSV positive.

d) In any case of missing RSV RNA viral load result in UTM, the participant is assumed to be RSV positive, regardless of Biofire result.

e) For viral load assay, either RSV-A or RSV-B positivity is considered as RSV positive for deriving the Full Analysis Positive Set. A patient with either RSV-A viral load or RSV-B viral load ≥ LLOQ should be included in the Virology Analysis Set.

3) Combined RSV Viral Load Calculation:

The calculation of combined RSV results in valid samples (when RNase P is positive from the same accession number as RSV-A and RSV-B) is summarized in the table below.

Baseline RSV Subtype Classification	**Combined RSV Formula applied to all baseline and post-baseline samples**
RSV-A/B Coinfection	Combined RSV = RSV-A imputed + RSV-B imputed
RSV-A only	Combined RSV = RSV-A imputed only
RSV-B only	Combined RSV = RSV-B imputed only
Not Determined*	Combined RSV = Blank

* Both RSV-A and RSV-B values at baseline are negative, missing or invalid.

RNase P is a quality check of the sample and should always be positive if the sample was collected correctly. If it is negative, we cannot trust the results of the sample and RSV-A/B should be considered invalid. The first step is to determine if RNase P is positive and negative. If positive, then RSV subtype is based on RSV-A and RSV-B character/numeric values reported (compared to LLOQ if needed).

4) The RSV Viral Load (copies/mL) of Combined RSV results will be displayed in the listing per rule below.

RSV-B / **RSV-A**	**Numeric Result in RSV-B**	**RSV-B Text = "TD"**	**RSV-B Text = "TND"**
Numeric Result in RSV-A	Combined Numeric Result	Numeric Result in RSV-A + Imputed Numeric Result in RSV-B	Numeric Result in RSV-A
RSV-A Text = "TD"	Numeric Result in RSV-B + Imputed Numeric Result in RSV-A	"TD"	"TD"
RSV-A Text = "TND"	Numeric Result in RSV-B	"TD"	"TND"

TD = target detected, TND = target not detected.

5) A general rule to handle samples (including viral load, infectious viral titer, and Biofire multiplex) under the following conditions.

Condition	Exclude from Qualitative analysis (Positive/Negative)	Exclude from Quantitative analysis
RNase P negative	Yes	Yes
Samples collected after rescue medication* received	Yes	Yes
wrong buffer[$]	No (but Yes if IVT)	Yes
aliquot<5	No	Yes
quantitative results unreliable	No	Yes
Participants with low combined RSV VL < 4 log10 copied/mL in UTM at baseline	Yes (if IVT)	Yes (if IVT)

* Samples collected after receiving rescue medication should be excluded from both qualitative and quantitative analysis.
$ Infectious Viral Titer (IVT) samples should be excluded from both analyses, while viral load samples should be excluded from quantitative analysis only.

6) RSV rescue medications
Details of RSV rescue medications are provided in the table below.

Drug Class	Dictionary Level	Preferred Term Codes	Prohibited Ingredient, PREF
Sisunatovir	PREF	15229401001	SISUNATOVIR
Zelicapavir (EDP-938)	PREF	N/A	N/A
Ribavirin	PREF	00816701001	RIBAVIRIN
Favipiravir	PREF	06325301001	FAVIPIRAVIR
Presatovir	PREF	08955601001	PRESATOVIR
Lumicitabine	PREF	09305701001	LUMICITABINE
Rilematovir	PREF	15227101001	RILEMATOVIR
Enzaplatovir	PREF	09305001001	ENZAPLATOVIR
Ziresovir	PREF	15917301001	ZIRESOVIR
Sinogen	PREF	06449501001	INTERFERON ALFA-1B
Interferon Alpha	PREF	05982601001	INTERFERON ALFA
RSV immunoglobulin	PREF	N/A	N/A
Palivizumab	PREF	01462801001	PALIVIZUMAB
Nirsevimab	PREF	15923101001	NIRSEVIMAB
Clesrovimab	PREF	N/A	N/A
Gontivimab	PREF	N/A	N/A
Suptavumab	PREF	09308801001	SUPTAVUMAB
Inarigivir soproxil	PREF	16431601001	INARIGIVIR SOPROXIL

Drug Class	Dictionary Level	Preferred Term Codes	Prohibited Ingredient, PREF
Danirixin	PREF	07842001001	DANIRIXIN
Motavizumab-YTE	PREF	06258001001	MOTAVIZUMAB
Asvasiran	PREF	08683201001	ASVASIRAN
Chlorpheniramine maleate	PREF	00072502001	CHLORPHENAMINE MALEATE
Asapiprant	PREF	N/A	N/A
Mindeudesivir hydrobromide	PREF	16035801001	DEUREMIDEVIR HYDROBROMIDE
Astodrimer	PREF	08634401001	ASTODRIMER
Respiratory syncytial virus immune globulin intravenous (RSV-IGIV)	PREF	07371201001	IMMUNOGLOBULIN ANTI RESPIRATORY SYNCYTIAL VIRUS


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