Enanta Pharmaceuticals

EDP 938-103

A PHASE 2B, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY EVALUATING THE EFFECTS OF EDP-938 IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS WITH ACUTE RESPIRATORY SYNCYTIAL VIRUS INFECTION OF THE UPPER RESPIRATORY TRACT

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Statistical Analysis Plan

Version: Final 1.0

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List of Abbreviations

AE	adverse event
ALC	absolute lymphocyte count
ANC	absolute neutrophil count
ATC	Anatomical Therapeutic Chemical
AUC	area under the curve
BLQ	below the limit of quantitation
BMI	body mass index
BUN	blood urea nitrogen
CBIA	cell-based infectivity assay
CMH	Cochran Mantel-Haenszel
CI	confidence interval
CNI	calcineurin inhibitor
CTMS	Clinical Trial Management System
CYP	cytochrome P450
DMC	Data Monitoring Committee
EAC	Endpoint Adjudication Committee
ECG	electrocardiogram
eCOA	electronic clinical outcome assessment
eCRF	electronic case report form
eGRF	estimated Glomerular Filtration Rate
EOS	End-of-Study
EOT	End-of-Treatment
[redacted]	
FSH	follicle-stimulating hormone
HCT	hematopoietic cell transplant
HDPE	high-density polyethylene
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICU	intensive care unit
IRT	interactive response technology
ITT	intent-to-treat
IWRS	Interactive Web Response System
LLOQ	lower limit of quantitation
LOD	lower limit of detection
LRTC	lower respiratory tract complication
LRTI	lower respiratory tract infection
MAARI	medically attended acute respiratory infection
MDRD	Modification of Diet in Renal Disease
MedDRA	Medical Dictionary for Regulatory Activities
mITT	modified intent-to-treat
mTOR	mammalian target of rapamycin
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NRR	Not reportable result

PK	pharmacokinetic(s)
PP	per protocol
PT	preferred term
QD	once daily
QTcF	QT interval corrected for heart rate according to Fridericia
RAV	resistance-associated variant
RBC	red blood cell count
RSV	respiratory syncytial virus
RT-qPCR	quantitative reverse transcription polymerase chain reaction
SAE	serious adverse event
SAF	safety
SAP	statistical analysis plan
SD	standard deviation
SE	standard error
SOC	system organ class
TEAE	treatment-emergent adverse event
TD	Target detected
TND	Target not detected
TSS	total symptom score
ULN	upper limit of normal
URTI	upper respiratory tract infection
WBC	white blood cell count
WHO	World Health Organization

1 Introduction

Respiratory syncytial virus is the leading cause of lower respiratory tract infection (LRTI) and presents a significant health challenge in infants, small children, elderly, and immunocompromised patients, such as those who have received HCT (*Falsey et al., 2005; Hall et al., 2009; Shook and Lin, 2017; Khawaja and Chemaly, 2019*). Respiratory syncytial virus is one of the most common community acquired respiratory viruses that may lead to death in HCT recipients, second only to influenza (*Khawaja and Chemaly, 2019*). The use of ribavirin has been associated with clinical benefit (e.g., reduced rates of progression from upper to lower respiratory tract infection and decreased mortality) in observational studies and case series. Currently, there is no vaccine or highly effective treatment available for RSV.

To address the unmet medical need for more effective antiviral therapies for RSV and based on the promising early nonclinical safety and pharmacological profile, Enanta Pharmaceuticals, Inc. is investigating EDP-938 in humans as a potential treatment for RSV infection. This Phase 2b study, EDP-938-103, is a randomized, double-blind, placebo-controlled, multicenter study designed to assess the efficacy, safety, and tolerability of EDP-938 compared with placebo in adult hematopoietic cell transplant (HCT) recipients with an acute RSV infection and symptoms of an upper respiratory tract infection (URTI).

This statistical analysis plan (SAP) is based upon the protocol (version 8.0, dated 7 March 2023) for this Phase 2b clinical study, and is prepared in compliance with *International Conference on Harmonisation (ICH) E3, E6 and E9*. Furthermore, this SAP contains definitions for analysis sets, derived variables, and statistical methods and data presentations for the analysis of efficacy and safety endpoints.

The study was terminated on September 12, 2023, due to slow enrollment. The decision was made by the sponsor. This statistical analysis plan describes the analyses that will be conducted based on the data collected up until the study terminated. The changes from the originally planned analyses in the protocol is described in Section 12.

2 Objectives

2.1 Primary Objective

- To evaluate the effect of EDP-938 on the development of lower respiratory tract complication (LRTC) in HCT subjects with an acute RSV infection of the upper respiratory tract

2.2 Secondary Objectives

- To evaluate the effect of EDP-938 on RSV viral load as measured by quantitative reverse transcription polymerase chain reaction (RT-qPCR) of nasopharyngeal swab samples
- To evaluate the effect of EDP-938 on progression to respiratory failure or all-cause mortality

- [redacted]
- To evaluate the pharmacokinetics (PK) of EDP-938 [redacted]
- To evaluate the safety and tolerability of EDP-938

[redacted]

3 Investigational Plan

3.1 Overall Study Design and Plan

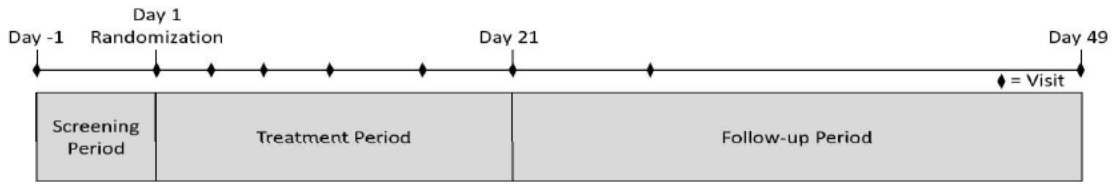
This is a Phase 2b, randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of EDP-938 in HCT recipients with acute RSV infection and symptoms of URTI.

The study has 3 periods:

- Screening Period will occur from Day -1 to Day 1. During this period, subjects will review and sign the ICF. Subjects will undergo screening assessments. Screening should be completed as soon as possible, and the subject will be randomized and administered the first dose of study drug within 24 hours of signing the ICF. A subject will be considered enrolled at the time of randomization.
- Treatment Period will begin with the first dose of study drug on Day 1 and will conclude with the End-of-Treatment (EOT) Visit on Day 21.
- Follow-up Period for safety will begin following the last dose of study drug and will conclude at the End-of-Study (EOS) visit on Day 49, 28 days following the last dose of study drug.

An overview of the study design is shown in Figure 1. Study site visits and assessments are detailed in the Schedule of Study Procedures (Appendix 14.1).

Figure 1: Study Design



3.2 Study Endpoints

3.2.1 Primary Endpoint

- Incidence of LRTC through Day 28 defined as at least one of the following as determined by the Endpoint Adjudication Committee
  - LRTI by RSV
  - LRTI as secondary bacterial pneumonia
  - LRTI by unusual pathogens
  - LRTC of unknown etiology

3.2.2 Secondary Endpoints

- Change in RSV RNA viral load from Baseline through Day 49 in nasopharyngeal swab samples by RT-qPCR
- Incidence of subjects with RSV RNA viral load below the limit of detection in subjects receiving EDP-938 through Day 49
- Plasma PK concentrations of EDP-938
- Safety endpoints include, but are not limited to, adverse events (AEs), serious adverse events (SAEs), vital sign measurements, pulse oximetry measurements, and clinical laboratory test results (including chemistry, hematology, and urinalysis)

3.3 Treatments

EDP-938 drug product tablets and the corresponding placebo tablets are supplied as 150 mg tablets and 200 mg tablets in [redacted]

Following randomization on Day 1, subjects will receive the first dose of EDP-938 or placebo orally while at the study site. After the first dose, subjects will be instructed to take the study drug orally once daily (QD) on each of the 20 subsequent days. [redacted]

- [redacted]
- [redacted]
- [redacted]

Subjects will be instructed to take the study drug at approximately the same time every day (±1 hour).

[redacted]

4 General Statistical Considerations

All analyses will be conducted using SAS Version 9.4 or higher.

Continuous data will be described using descriptive statistics (i.e. n, mean, standard deviation (SD), median, 25th percentile, 75th percentile, minimum, and maximum). For the summary statistics of all numerical variables unless otherwise specified, minimum and maximum will be displayed to the same level of precision as reported. Mean and median will be displayed to one level of precision greater than the data collected. Standard deviation / standard error (SE) will be displayed to two levels of precision greater than the data collected. If the precision of the values being summarized are too large (e.g. 3 or more decimal places), then limit the precision to two decimal places and follow the rules previously stated above. For derived data, the precision of values will be determined on a case-by-case basis. If n=0, then display n and leave all other statistics blank. If n=1, display "N/A" for SD and SE.

Categorical data will be described using the subject count and percentage in each category. When count data are presented, the percentage will be suppressed when the count is zero. A row denoted "Missing" will be included in count tabulations where specified on the shells to account for dropouts and missing values where applicable. The denominator for all percentages will be the number of subjects in that treatment within the analysis set of interest, unless otherwise specified. Non-zero percentages will be rounded to one decimal place, except 100% will be displayed without any decimal places.

Summary Tables will be presented by treatment group. Tables values for treatment group will be labelled as follows: • "EDP-938" • "Placebo". Models will include stratification factors, ribavirin treatment (present or absent) and ALC (<200 or ≥200 cells/μL), unless an insufficient amount of data exists where convergence or the analysis cannot be performed.

All subject data, including those derived, will be presented in individual subject data listings. Dates will be shown in subject listings as they have been recorded. Unless otherwise stated, unscheduled visit results will be included in date/time chronological order, within subject listings only. All listings will be sorted by subject number, date/time and visit. The treatment group (randomized) as well as subject's sex and age will be stated on each listing. Unless otherwise stated, data listings will be based on all subjects randomized.

When no data are available for a table or listing, an empty page with the title will be produced with suitable text (e.g., "There are no records for this table/listing."). For analyses where convergence or the analysis cannot be performed, "NC" (not calculable) will be presented in summary tables.

Unless otherwise specified, baseline will be defined as the last non-missing measurement collected on or before the date of the first dose of study treatment. For subjects who are randomized, but not treated, the baseline will be defined as the last non-missing measurement on or before the date of randomization. The date of first dose will be collected on the Day 1 Study Drug eCRF and the date of last dose will be the date collected on the End of Treatment eCRF.

For the reporting of this study both CDISC SDTM (SDTM Implementation Guide version 3.2) and ADaM (ADaM Implementation Guide version 1.1) standards will be applied. A subject will be considered to have completed the study after his/her attendance at the last planned study visit (Day 49 ± 2 days), or the last unscheduled visit (if any occur), as applicable. For each subject his or her study completion status (Yes/No) is recorded on the End of Study CRF.

4.1 Sample Size

When the study was terminated, there were 9 subjects randomized.

4.2 Randomization, Stratification, and Blinding

Subjects who had completed screening assessments and were eligible for participation in the study were randomized to blinded treatment before the first dose of study drug (Day 1) in a 2:1 ratio to [redacted] EDP-938 or placebo administered orally for 21 days. Subject

randomizations were stratified by ribavirin treatment (present or absent) and ALC (<200 or ≥200 cells/µL) at Screening. Assignments to treatment groups were determined by a computer-generated random sequence using an IWRS. The IWRS was used to assign investigational product to each subject. A unique four-digit randomization identifier was assigned by interactive response technology (IRT), which will become the subject number and be used to identify the subject throughout the study.

The study was double-blinded, meaning subjects, investigators, site staff and the CRO/Sponsor study team were blinded to treatment assignment until the completion of the study. During the study, investigators, site personnel, and blinded CRO/Sponsor study team did not have access to results for individual subjects that could impact clinician assessments, including results for RSV viral load, confirmatory respiratory pathogen panel testing, biomarkers, and PK.

4.3 Analysis Populations

4.3.1 Intent-to-Treat (ITT)

The intent-to-treat (ITT) population will include all subjects who receive at least one dose of study drug. All subjects in the ITT population will be analyzed according to the treatment as randomized. The ITT population will be used for the primary efficacy analysis [redacted]

4.3.2 Modified Intent-to-Treat by RT-qPCR (mITT by RT-qPCR)

The modified intent-to-treat by RT-qPCR (mITT by RT-qPCR) population will include all subjects in the ITT population, excluding subjects who have undetectable or missing RSV viral load by RT-qPCR at baseline. The mITT by RT-qPCR population will be used for efficacy analysis on RSV viral load by RT-qPCR. This population will exclude subjects with baseline value reported as TND (target not detected), NOR (No valid result), QNS (Quantity Not Sufficient) or not done.

4.3.3 Modified Intent-to-Treat by CBIA (mITT by CBIA)

The modified intent-to-treat by CBIA (mITT by CBIA) population will include all subjects in the ITT population, excluding subjects who have undetectable or missing RSV viral load by CBIA at baseline. The mITT by CBIA population will be used for efficacy analysis on RSV viral load by CBIA. This population will exclude subjects with baseline value reported as TND (target not detected), NRR (not reportable result) or not done.

4.3.4 Safety (SAF)

The safety (SAF) population will include all subjects who received at least one dose of study drug. All subjects in the safety population will be analyzed according to the treatment actually received.

4.3.5 Pharmacokinetic (PK)

The pharmacokinetic (PK) population will include all subjects receiving active study drug and having any measurable plasma concentration of study drug at any timepoint.

4.4 Data Handling Strategy

4.4.1 Study Days and Visit Windows

Study day is defined as the number of days from the date of first dose. Day 1 is the date of the first dose. For assessments or events that occur after the first dose date, study day is calculated as the date of interest minus first dose date plus 1 day. For assessments or events that occur before the first dose date, study day is calculated as the date of interest minus the first dose date.

Analysis visit windows are described in the tables below. Analysis visits are based on nominal scheduled visits and will be used for by-visit analyses or summaries unless otherwise specified in the respective analysis sections. Unscheduled visits and visits performed for early discontinuation will not be included in the by-visit summary or analyses.

- Unscheduled visits including repeat central laboratory assessments for the EOS visit to follow an AE for resolution will not be included in the by-visit analyses/ summaries, but will be included in the listings and other types of analyses/summaries as applicable (e.g. AUC, time to event and treatment emergent safety abnormalities any time post-baseline). For subjects who discontinues study treatment, they should complete a EOT visit and this visit will be labeled as “Early Disc/EOT”. For these subjects, they should also complete FU1 visit and FU2 visit, and these visits will be labeled as “Early Disc/FU1’ and “Early Disc/FU2”.
- For subjects who completes study treatment and discontinues study before Day 28, they should complete FU1 visit and this visit will be labeled as “Early Disc/FU1’. For subjects who discontinues study between Day 28 and Day 49, they should complete FU2 visit and this visit will be labeled as “Early Disc/FU2’.

Vital signs and safety laboratory tests:

Analysis Visit #	Analysis Visit Label	Target Day	Derivation
1	Day 1	1	Based on nominal visit of V1
4	Day 4	4	Based on nominal visit of V2
7	Day 7	7	Based on nominal visit of V3
11	Day 11	11	Based on nominal visit of V4
16	Day 16	16	Based on nominal visit of V5
21	Day 21	21	Based on nominal visit of V6 if subject completes treatment

28	Day 28	28	Based on nominal visit of FU V1 if subject completes treatment and last visit is FU V2.
97	Early Disc/EOT	NA	Based on nominal visit of V6 if subject discontinues treatment
98	Early Disc/FU1	NA	Based on nominal visit of FU V1 if subject discontinues treatment or last visit is FU V1.

RSV viral load by both RT-qPCR and CBIA:

Analysis Visit #	Analysis Visit Label	Target Day	Derivation
1	Day 1	1	Based on nominal visit of V1
4	Day 4	4	Based on nominal visit of V2
7	Day 7	7	Based on nominal visit of V3
11	Day 11	11	Based on nominal visit of V4
16	Day 16	16	Based on nominal visit of V5
21	Day 21	21	Based on nominal visit of V6 if subject completes treatment
28	Day 28	28	Based on nominal visit of FU V1 if subject completes treatment and last visit is FU V2.
49	Day 49	49	Based on nominal visit of FU V2 if subject completes treatment and study
97	Early Disc/EOT	NA	Based on nominal visit of V6 if subject discontinues treatment
98	Early Disc/FU1	NA	Based on nominal visit of FU V1 if subject discontinues treatment or last visit is FU V1.
99	Early Disc/FU2	NA	Based on nominal visit of FU V2 if subject discontinues treatment or study.

ECG:

Analysis Visit #	Analysis Visit Label	Target Day	Derivation
-1	Screening	-1	Based on nominal visit of Screening
4	Day 4	4	Based on nominal visit of V2
11	Day 11	11	Based on nominal visit of V4
21	Day 21	21	Based on nominal visit of V6 if subject completes treatment.
28	Day 28	28	Based on nominal visit of FU V1 if subject completes treatment and last visit is FU V2.
97	Early Disc/EOT	NA	Based on nominal visit of V6 if subject discontinues treatment
98	Early Disc/FU1	NA	Based on nominal visit of FU V1 if subject discontinues treatment or last visit is FU V1.

PK:

Analysis Visit #	Analysis Visit Label	Target Day	Timepoint* Assessment	Derivation
1	Day 1	1	1	Based on nominal visit of V1
1	Day 1	1	2	Same as above
4	Day 4	4	1	Based on nominal visit of V2
7	Day 7	7	1	Based on nominal visit of V3
7	Day 7	7	2	Same as above
11	Day 11	11	1	Based on nominal visit of V4
16	Day 16	16	1	Based on nominal visit of V5

21	Day 21	21	1	Based on nominal visit of V6 if subject completes treatment
21	Day 21	21	2	Same as above
97	Early Disc/EOT	NA		Based on nominal visit of V6 if subject discontinues treatment

* On Day 1, Day 7, and Day 21, two plasma PK samples will be collected (one predose and one postdose) and thus are assigned as Timepoint 1 and 2. At all other visits, only predose samples will be collected.

4.4.2 Missing Date Imputation

Imputation rules for missing or partial AE start/end dates are defined as:

- Only Day of AE start date is missing:
  - If the AE start year and month are the same as that for the first dose date, then:
    - If the full (or partial) AE end date is NOT before the first dose date or AE end date is missing, then impute the AE start day as the day of first dose date.
  - Otherwise, impute the AE start day as 1.
- If Day and Month of AE start date are missing:
  - If AE start year = first dose year, then:
    - If the full (or partial) AE end date is NOT before the first dose date or AE end date is missing, then impute the AE start Month and Day as the Month and Day of first dose date.
  - Otherwise, impute the AE start MONTH as January and the DAY as 1.
- If Year of AE start date is missing:
  - If the year of AE start is missing or AE start date is completely missing, then query site and leave as missing.
- For missing and partial adverse event end dates, imputation will be performed as follows:
  - If only the day of the month is missing, the last day of the month will be used to replace the missing day.
  - If the day and month are missing or a date is completely missing, it will be considered as missing.

Imputation rules for missing or partial medication/therapy start/stop dates are defined below:

- If only Day of CM start date is missing:
  - If the CM start year and month are the same as that for the first dose date, then:

        - If the full (or partial) CM end date is NOT before the first dose date or CM end date is missing, then impute the CM start day as the day of first dose date.
    - Otherwise, impute the CM start day as 1.
- If Day and Month of CM start date are missing:
    - If CM start year = first dose year, then:
        - If the full (or partial) CM end date is NOT before the first dose date or CM end date is missing, then impute the CM start Month and Day as the Month and Day of first dose date.
    - Otherwise, impute the CM start MONTH as January and the DAY as 1.
- If Year of CM start date is missing:
    - If the year of CM start is missing or CM start date is completely missing, then query site and leave as missing.
- For missing and partial CM end dates, imputation will be performed as follows:
    - If only the day of the month is missing, the last day of the month will be used to replace the missing day.
    - If the day and month are missing or a date is completely missing, it will be considered as missing.

5 Subject Disposition

5.1 Disposition

A summary of the analysis populations includes the number and percentage of subjects in each analysis population (ITT, mITT by RT-qPCR, mITT by CBIA, SAF, and PK) by treatment group and overall. The number and percentage of subjects excluded from each analysis population and the reasons for exclusion will also be presented. All percentages will be based on the number of subjects randomized.

Subject disposition will be summarized by treatment group and overall for all subjects who provided informed consent. A disposition of subjects includes the number and percentage of subjects for the following categories: subjects who were randomized, subjects who completed study treatment, subjects who discontinued study treatment, subjects who completed the study, subjects who discontinued from the study. All percentages will be based on the number of subjects randomized. The reasons for discontinuation of study treatment and study participation will also be summarized in this table.

The reason for discontinuation of study treatment or study participation may include any of the following: adverse event, lack of efficacy, lost to follow-up, pregnancy, protocol deviation, study terminated by sponsor, withdrawal by subject, physician decision, COVID-19, or other reason.

Subject disposition data and exclusions from analysis populations will also be presented in a listing.

5.2 Protocol Deviations

All protocol deviations (both significant and non-significant) were entered and tracked in [redacted] Clinical Trial Management System (CTMS) by the study team throughout the conduct of the study in accordance with [redacted] Study Deviation Rules Document. A significant deviation is any deviation that may affect primary efficacy and safety assessments (as applicable), the safety or mental integrity of a subject, or the scientific value of the trial.

Data will be reviewed by the study team prior to unblinding and closure of the database to ensure all significant deviations are captured and properly categorized.

Significant protocol deviations will be summarized by treatment group and overall based on randomized subjects. A separate listing will be provided for significant protocol deviations and non-significant protocol deviations.

6 Demographics and Baseline Characteristics

6.1 Demographics

A summary of demographics and baseline information will be presented by treatment group and overall for all subjects in the safety population.

The demographic characteristics consist of age, sex, race, and ethnicity.

The baseline characteristics consist of baseline height, baseline weight, baseline body mass index, smoking history, ribavirin treatment at screening (stratification factor), absolute lymphocyte count (ALC) at screening (stratification factor), absolute neutrophil count (ANC) on Day 1, RSV subgroup, [redacted] RSV viral load by RT-qPCR and CBIA, co-pathogens detected on Day 1, hospitalization status on Day 1 [redacted]. Body mass index is calculated as (body weight in kilograms) / (height in centimeters / 100)^2. RSV subgroup is determined by an RSV A/B RT-qPCR assay and co-pathogens are determined by a respiratory pathogen panel at the central laboratory. The baseline RSV type category is derived by algorithm described in Section 8.2.1.

Age (years), baseline height (cm), baseline weight (kg), baseline BMI (kg/m^2), [redacted] RSV viral load as measured by RT-qPCR ($\log_{10}$ copies/mL) and CBIA ($\log_{10}$ PFU/mL) will be summarized using descriptive statistics. The number and percentage of subjects by age group (< 65, ≥ 65 years), sex (Male, Female), race (White, African American, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, Other), ethnicity (Hispanic or Latino, Not Hispanic or Latino), smoking history (Current, Previous, Never), ribavirin treatment at screening (Present, Absent), ALC at screening (<200, ≥200 cells/µL), ANC on Day 1 (<500, ≥500 cells/µL), RSV subgroup (RSV A, RSV B, Undetectable, Missing), co-pathogens detected on Day 1 (e.g., Adenovirus, Parainfluenza virus, SARS-CoV-2), hospitalized on Day 1 (Yes,

No), [redacted], and subjects with any medical conditions will also be reported. Percentages will be based on the total number of subjects in the safety population.

Subject demographic and baseline characteristics will also be presented in a listing. Additionally, the RSV test information collected at screening (i.e. RSV test date, RSV test type, manufacturer name of RSV test, RSV test result, number of days between RSV test and first dose) will be presented in a separate listing.

6.2 Medical History

6.2.1 General Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 or higher. The number and percentage of subjects with any medical history will be summarized overall and for each system organ class and preferred term. Percentages will be calculated based on number of subjects in the safety population.

Subject medical history data including specific details, will also be presented in a listing.

6.2.2 Hematopoietic Cell Transplant History

Hematopoietic cell transplant (HCT) history will be collected at screening and will consist of donor type, cell source, date of transplant, conditioning regimen prior to HCT, diagnosis for which HCT was received, CMV seropositive status, and acute or chronic graft-vs-host disease. HCT history will be summarized in a table by treatment group and overall. Percentages will be based on the number of subjects in the safety population.

HCT history data will also be presented in a listing.

7 Treatments and Medications

7.1 Prior and Concomitant Medications

All medications taken within 1 month of signing informed consent and during the study throughout the end of the study will be collected on the CRF. All medications will be coded according to the World Health Organization (WHO) Drug Dictionary (WHODrug Global-B3 202009 or later).

Prior medications are defined as those medications with a start date prior to the date of first dose of study drug. Concomitant medications are defined as any medications with a start date on or after the date of first dose of study drug or any medications with a start date prior to the date of first dose and a stop date after the date of first dose. Furthermore, a medication could be labeled as both a prior and concomitant medication if it was started prior to the first dose of study drug and continued after the first dose of study drug.

The number and percentages of subjects with at least one prior medication will be summarized by treatment group and overall. The number and percentages of all prior medications will be summarized by treatment group and overall and listed by Anatomical Therapeutic Chemical (ATC) level 2 and preferred term. All summaries will be performed using the safety population.

The number and percentages of subjects with at least one concomitant medication will be summarized by treatment group and overall. The number and percentages of all concomitant medications will be summarized by treatment group and overall and listed by Anatomical Therapeutic Chemical (ATC) level 2 and preferred term. All summaries will be performed using the safety population.

Prior and concomitant medications, including prohibited medication, will also be presented in a listing. Details for imputing missing or partial start and/or stop dates of medications are described in Section 4.4.2.

7.2 Prior and Concomitant Therapies

Prior and concomitant therapies include surgical interventions, procedures, or non-medication treatments (e.g. supplemental oxygen). All reported therapies will be coded using the MedDRA Version 23.1 or higher and classified by system organ class (SOC) and preferred term (PT).

Prior therapies are defined as those therapies with a start date prior to the date of first dose of study drug. Concomitant therapies are defined as any therapies with a start date on or after the date of first dose of study drug or any therapies with a start date prior to the date of first dose and a stop date after the date of first dose.

Both prior and concomitant therapies will be presented in a listing. Details for imputing missing or partial start and/or stop dates of medications are described in Section 4.4.2.

7.3 Study Treatments

The study drug administration data collected from eCRF will be listed.

8 Efficacy and Pharmacokinetics Analysis

Efficacy analysis on LRTC [redacted] will be based on ITT population. The efficacy analysis on RSV viral load by RT-qPCR will be based on mITT by RT-qPCR population, The efficacy analysis on RSV viral load by CBIA will be based on mITT by CBIA population. Missing data will not be imputed unless otherwise specified. Relevant subject data listings will be provided to support all efficacy analyses.

8.1 Primary Efficacy Endpoint

The primary endpoint is the proportion of LRTC through Day 28, defined as one of the following, as determined by the Endpoint Adjudication Committee (EAC):

- LRTI by RSV
- LRTI as secondary bacterial pneumonia
- LRTI by unusual pathogens
- LRTC of unknown etiology

The EAC reviewed relevant clinical data and source documentation to determine whether a LRTC occurred, the type and date of onset of any LRTC. Details of the adjudication process were provided to the EAC in an EAC charter. This EAC charter defined the EAC membership, EAC's responsibility, data to be provided to the EAC, review process, documentation of EAC decision, meeting logistics, and meeting frequency.

8.1.1 Primary Analysis

The number and proportion of subjects who developed LRTC through Day 28 will be summarized for each treatment group for ITT population. Subjects with missing LRTC data will be considered having no LRTC event. The LRTC data will also be listed.

8.2 Secondary Efficacy Endpoints

8.2.1 RSV viral load AUC by RT-qPCR from Baseline (Day 1) through Day 49

The RSV viral load will be measured in nasopharyngeal swabs by quantitative RT-qPCR at the following scheduled visits: Days 1, 4, 7, 11, 16, 21, 28, and 49. Viral load values reported as TD (Target detected) are samples with viral RNA concentrations equal and above the LOD (limit of detection) (TD $\geq$ LOD) and below the LLOQ (lower limit of quantification). (TD < LLOQ). For analysis purpose, TD will be set to the average of LOD and LLOQ Viral load values reported as TND (Target Not Detected, value below LOD) will be set to zero. Viral load data will be transformed using a $\log_{10}$ scale before analyses. If zero values are observed, the log transformed value will be set to zero. For the RT-qPCR assay used for detection and quantification of RSV A and RSV B, the LLOQ is 1000 copies/mL for RSV A and 250 copies/mL for RSV B and the LOD is 620 copies/mL for RSV A and 80 copies/mL for RSV B.

The RSV type of each subject will be decided at baseline based on the RT-qPCR test. The baseline RSV by RT-qPCR result is from the nasopharyngeal swab sample taken after randomization and prior to first dose on Day 1. After the imputation of TD, TND, and $\log_{10}$ transformation, if the baseline RSV A viral load is greater than RSV B viral load, the baseline RSV type is classified as RSV A. And if the baseline RSV B viral load is greater than RSV A viral load, the baseline RSV type is classified as RSV B.

After the categorization of baseline RSV type, only RSV values from the same baseline RSV type will be selected for postbaseline values to be used for analyses.

The AUC of RSV viral load by RT-qPCR will be calculated using the trapezoid rule (*Matthews et al., 1990*). To calculate AUC, at least two non-missing data points on the RSV by RT-qPCR curve are needed. The AUC will be calculated based on available individual assessments of viral

load collected at each visit (Days 1, 4, 7, 11, 16, 21, 28, and 49) and the actual date/time of each assessment will be used for the calculation. For the baseline viral load (Day 1), time is set as 0. For each assessment post first dose, the actual time in days is computed as difference between the date/time of the assessment and the date/time of the first dose. The AUC is also standardized to 49 days by multiplying $49/t_{last}$ where t_{last} is the actual time in days of the last available assessment up to Day 49 visit.

The descriptive statistics for the RSV viral load AUC by RT-qPCR from Day 1 to Day 49 will be presented by treatment group based on the mITT by RT-qPCR population. The RSV viral load by RT-qPCR data will be listed.

8.2.2 Change from Baseline in RSV viral load by RT-qPCR over time

Observed and change from baseline values for RSV viral load by RT-qPCR will be summarized with descriptive statistics by visit (Days 1, 4, 7, 11, 16, 21, 28, and 49) for each treatment group based on mITT by RT-qPCR population and will include the number of non-missing measurements, mean, standard deviation, median, minimum, 25th percentile, 75th percentile, and maximum.

8.2.3 Proportion of subjects with RSV viral load by RT-qPCR below the LOD over time

The proportion of subjects with RSV viral load by RT-qPCR below the limit of detection (LOD) will be summarized by visit (Days 4, 7, 11, 16, 21, 28, and 49) for each treatment group based on mITT by RT-qPCR population.

[redacted]

[redacted]

8.4 PK Endpoints

8.4.1 Plasma PK concentrations of EDP-938 [redacted]

On Day 1, Day 7, and Day 21, two samples will be collected: one predose, collected within 1 hour before dosing (preferably within 30 minutes of dosing if possible); and at the same approximate time as that of the nasopharyngeal swab collection and one postdose, collected 1 to 3 hours postdose. At all other visits (Days 4, 11, and 16), one predose plasma PK sample will be collected at the same approximate time as that of the nasopharyngeal swab collection. Time and date of collection will be recorded on the Plasma PK Sample Collection eCRF.

For subjects in the PK analysis set, the concentration data for EDP-938 and each [redacted] will be summarized by visit (Days 1, 4, 7, 11, 16, and 21) and timepoint (predose or postdose). Concentrations that are below the limit of quantitation (BLQ) will be treated as zero for the computation of descriptive statistics. If more than 50% of subjects have concentration values below BLQ, descriptive statistics will not be presented except for maximum and BLQ will be displayed for mean and minimum. The number of observations, arithmetic mean, SD, % coefficient of variation (%CV), median, minimum, maximum, geometric mean, and %CV of the geometric mean (%GCV) will be displayed.

Individual data will be presented in a listing.

9 Safety Analysis

All safety analyses will be conducted using the Safety (SAF) population, where subjects will be analyzed according to the treatment actually received.

9.1 Adverse Events

Adverse events (AEs) will be coded using the MedDRA Version 23.1 or higher and classified by SOC and PT.

AEs will be classified as pre-treatment AEs and treatment emergent adverse events (TEAEs) and are defined as follows:

- A pre-treatment event is any event that meets the criteria for an AE/SAE and occurs after the subject signs the ICF but before receiving the first administration of study drug.
- A TEAE is defined as an AE occurring or worsening on or after the date of first dose of study drug.

A treatment-related AE will be defined as related if causality is related or possibly related. AEs where the causality is missing will be assumed to be related in table summaries.

TEAEs leading to study drug discontinuation will be identified as TEAEs with a study drug action taken of "Drug Withdrawn". TEAEs leading to death will be identified as TEAEs with an outcome of "Death Related to Adverse Event".

Adverse events (serious and non-serious) will be graded in accordance with the NCI-CTCAE scale as follows: Mild (Grade 1), Moderate (Grade 2), Severe (Grade 3), Life threatening (Grade 4), and Death (Grade 5). AEs with missing severity will be assumed to be severe in table summaries.

Details for imputing missing or partial start and/or stop dates of AEs are described in Section 4.4.2.

All summaries of AEs will be based on treatment-emergent adverse events (TEAEs) in the safety population. The following summaries of TEAEs will be provided by treatment group:

- An overall summary of TEAEs including the number of TEAEs and the number and percentage of subjects with any of the following: TEAEs, study drug related TEAEs, TEAEs of grade 3 or higher, TEAEs by maximum grade, TEAEs leading to study drug discontinuation, TEAEs leading to death, serious TEAEs, and study drug related serious TEAEs.
- TEAEs – by PT and SOC
- Study Drug-Related TEAEs - by PT and SOC
- TEAEs of Grade 3 or Higher - by PT and SOC
- TEAEs by Maximum Grade – by PT and SOC
- TEAEs leading to study drug discontinuation – by PT and SOC
- AEs leading to death – by PT and SOC
- Serious TEAEs – by PT and SOC
- Study Drug-Related Serious TEAEs – by PT and SOC

For the above summaries by SOC and PT, each subject is counted once within each unique category. For the summary by maximum severity, subjects who experience the same event several times, with different severity levels, will only be counted with the maximum severity.

AEs will be sorted in descending order of frequency of SOC based on the total of all treatment groups. Within each SOC, AEs will be sorted in alphabetical order of preferred terms.

Subject AEs will also be presented in a listing.

9.2 Clinical Laboratory Evaluations

Safety laboratory tests include chemistry, hematology, and urinalysis will be performed by a central laboratory on Days 1, 4, 7, 11, 16, 21, and 28. Estimated glomerular filtration rate (eGRF) will be calculated using the Modification of Diet in Renal Disease (MDRD) equation.

Summary tables for observed values and changes from baseline will be presented for clinical laboratory tests with numeric values by treatment group and visit for subjects in the safety population.

All safety laboratory data will be included in separate listings and all test values outside the normal range will be flagged.

9.2.1 Hematology

The following laboratory tests will be included: Hemoglobin, Hematocrit, Differential white blood cell count, percentage and absolute (basophils, eosinophils, lymphocytes, monocytes, neutrophils), Mean corpuscular hemoglobin, Mean corpuscular hemoglobin concentration, Mean corpuscular volume, Platelet count, Red blood cell count, White blood cell count, International normalized ratio, Prothrombin time, and Activated thromboplastin time.

9.2.2 Serum Chemistry

The following laboratory tests will be included: Alanine aminotransferase, Albumin, Alkaline phosphatase, Amylase, Aspartate aminotransferase, total and direct bilirubin, BUN, BUN/creatinine ratio, Calcium, Creatine kinase, Creatinine, Estimated glomerular filtration rate, Uric acid, Sodium, Potassium, Chloride, Bicarbonate, Phosphorus, Gamma glutamyl transferase, Total globulin, Glucose, Cholesterol, Triglycerides, Lactate dehydrogenase, Lipase, Total protein, Calcineurin and mTOR inhibitors.

9.2.3 Urinalysis

The following laboratory tests will be included: color and appearance, pH, specific gravity, bilirubin, glucose, ketones, leukocytes, nitrite, occult blood, protein, urobilinogen, microscopic examination (including red blood cells and white blood cells).

9.3 Vital Sign Measurements

Vital signs include heart rate (beats/min), respiratory rate (breaths/min), systolic and diastolic blood pressure (mmHg), body temperature (°C), weight (kg), and BMI (kg/m^2). Pulse oximetry

will be performed to measure oxygen saturation (%). Vital signs and pulse oximetry will be measured at Days 1, 4, 7, 11, 16, 21, and 28.

All vital sign and pulse oximetry data will be presented in a listing.

9.4 Physical Examination

A full physical examination will be performed at Screening and any subsequent examinations performed at the discretion of the investigator will be targeted to new signs and symptoms. Any abnormal findings should be captured directly on the medical history or AE pages directly as appropriate.

9.5 Electrocardiogram

All subjects will have a standard 12-lead electrocardiogram (ECG) performed locally during the study at Screening, Day 4, Day 11, Day 21, and Day 28.

ECG data includes heart rate, RR interval, PR interval, QRS duration, QT interval, and QT interval corrected for heart rate according to Fridericia (QTcF), etc.

ECG data for subjects will be presented in a listing.

10 Interim Analysis

No interim analysis was conducted.

11 Data Monitoring Committee (DMC)

An independent Data Monitoring Committee (DMC) was established to review the safety data throughout the study to ensure the safety of study subjects, the ethical continuation of the study, and provide recommendations regarding continuation or termination of the study. The DMC was headed by a DMC Chair and will include one or more physicians with expertise in transplant medicine. The DMC consisted of experts independent from the Sponsor.

The roles, responsibilities and rules governing operation of the DMC were discussed in full in the DMC charter, which was finalized prior to the administration of investigational product. The DMC charter defined the primary responsibilities of the DMC; guide its activities, its relationship with other study components, its membership, and the purpose and timings of its meetings. It provided the procedures for ensuring confidentiality, formal communication, and outline of the content of reports that will be provided by the DMC.

12 Changes in the Planned Analysis

The study was terminated early by sponsor on September 12, 2023. Due to the small number of subjects randomized into the study, it was decided a reduced data analysis will be provided. The statistical tests or large sample-based estimates defined in the protocol, such as Cochran Mantel-

Haenszel (CMH) test p-value, 95% CI for proportions, treatment difference estimates in proportions and its 95% CI, Cox proportional model estimate for hazard ratio and its 95% CI, Kaplan-Meier estimates will not be provided for treatment comparison purpose. The study exposure duration and compliance will not be calculated. The incidence of treatment-emergent laboratory tests, vital signs, or ECG will not be summarized. The summary of observed and change from baseline in vital sign and ECG will not be provided. [redacted]

In addition, the following endpoints defined in the protocol are deleted from this analysis plan. If the related raw data will still be listed, some details are provided as needed:

- Incidence of subjects who develop respiratory failure of any cause requiring mechanical ventilation (invasive or noninvasive) or all-cause mortality through Day 49
    - Respiratory failure events requiring mechanical ventilation can be identified based on the Concomitant Therapy eCRF where the response to the respiratory failure therapy question is Yes. Death events can be identified based on the Adverse Events eCRF where the outcome is checked as “Fatal” and/or severity as “Death”. The mechanical ventilation will be listed. The all cause mortality will be listed in AE listing.
- Time to RSV RNA viral load below the limit of detection
- Plasma PK concentrations of EDP-938 in relation to the following:
    - RSV RNA viral loads from Baseline through Day 49
    - [redacted]
- Incidence of subjects hospitalized or rehospitalized through Day 49
    - Hospitalization data will be listed. A subject will be considered being hospitalized or re-hospitalized if the subject has any hospitalization or re-hospitalization that starts or restarts on or after the first dose date.
- Incidence of medically attended acute respiratory infection (MAARI) through Day 49
    - The MAARI data will be listed. A subject will be considered as developing MAARI if the subject has any hospitalizations, home health visits, non-hospitalization visits, or receives any concomitant therapies related to MAARI that occur on or after the first dose date. The dates of the medical visits and therapy use related to MAARI were collected on the Hospitalization eCRF, Home Health Care Visit eCRF, MAARI Non-Hospitalization Visit eCRF, and the Concomitant Therapy eCRF, respectively.
- Incidence, duration and number of days free of supplemental oxygen requirement through Day 49
    - A subject will be considered as requiring supplemental oxygen if the subject was administered any supplemental oxygen on or after the first dose date. Dates of supplemental oxygen use were reported on the Concomitant Therapy eCRF. The available supplemental oxygen data will be listed.
- Duration of time of hospital stay and time in the ICU through Day 49
- Incidence of use of certain therapeutics including antibiotics, ribavirin, corticosteroids, and/or immunoglobulin through Day 49

    - The data for individual subjects who use certain therapeutics through Day 49 will be included in the concomitant medication listing.
- Emergence of EDP-938 resistance-associated variants (RAVs) in RSV obtained from nasopharyngeal swab samples
- RSV subgroup/genotype obtained from nasopharyngeal swab samples in relation to the following:
    - RSV viral load from Baseline through Day 49
    - [redacted]

13 References

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14 Appendices

14.1 Schedule of Study Procedures

Period	Screening	Treatment						Follow-up	
Visit	**Screening**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**FU V1 (EOT +1wk)**	**FU V2 (EOT +4wks)**
Day	**D-1 to D1 Screening**	**D1 Randomization[a]**	**D4**	**D7±1d**	**D11±1d**	**D16±1d**	**D21+1d EOT[b]**	**D28±1d**	**D49±2d EOS[b]**
Study site visit	X	X	X	X	X	X	X	X	X
Informed consent form	X								
Demographics, medical history[c]	X								
Smoking history	X								
Local RSV diagnostic test[d]	X								
Chest Imaging[e]	X								
Vital sign measurements and pulse oximetry[f]	X	X[g]	X	X	X	X	X	X	
Physical examination[h]	X	X[i]	X	X	X	X	X	X	
Safety laboratory tests[j]	X	X[k]	X	X	X	X	X	X	
Height[l]	X								
Weight and BMI[l]	X		X	X	X	X	X	X	
Pregnancy test[m]	X	X						X	X
FSH[n]		X							
12-Lead ECG (resting)	X		X		X		X	X	
Randomization[o]		X							
[redacted]	[redacted]								
Nasopharyngeal swab collection[q]		X	X	X	X	X	X	X	X
RSV serology collection		X						X	
Exploratory biomarker collection[r]		X					X	X	
Study drug dosing[s]		X	X	X	X	X	X		
Study drug accountability[t]		X	X	X	X	X	X		
PK sample collection[u]		X	X	X	X	X	X		
CNI and mTOR sample[v]		X	X	X	X	X	X	X	

Period	Screening	Treatment						Follow-up	
Visit	Screening	V1	V2	V3	V4	V5	V6	FU V1 (EOT +1wk)	FU V2 (EOT +4wks)
Day	D-1 to D1 Screening	D1 Randomization[a]	D4	D7±1d	D11±1d	D16±1d	D21+1d EOT[b]	D28±1d	D49±2d EOS[b]
Assess ICU admissions, hospitalizations, MAARI, standard of care test results, mechanical ventilation, and supplemental oxygen[w]		X	X	X	X	X	X	X	X
Prior/concomitant therapies[x]	X	X	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X	X	X

Abbreviations: BMI = body mass index; CNI = calcineurin inhibitors; D/d = Day/day; ECG = electrocardiogram; eCOA = electronic clinical outcome assessment; eCRF = electronic case report form; EOS = End-of-Study; EOT = End-of-Treatment; FLU-PRO = InFLUenza Patient-Reported Outcome; FSH = follicle-stimulating hormone; FU = follow-up; ICF = informed consent form; ICU = intensive care unit; MAARI = medically attended acute respiratory infection; mTOR = mammalian target of rapamycin; PK = pharmacokinetic; RSV = respiratory syncytial virus; V = visit.

Note: Refer to the Laboratory Manual for sample collection and processing details.

[a] Day 1 assessments to be performed in randomized subjects.

[b] Subjects who discontinue treatment early (i.e., before completing 21 days of dosing) should return to the study site within 24 hours from the last dose of study treatment to complete an EOT visit. They should then return to the clinic for the Follow-up Visit 1 (EOT + 1 week) and the EOS visit 4 weeks following the last dose of the study drug. Subjects who discontinue the study before Day 28 should return to the site within 48 hours to complete Follow-up Visit 1 (EOT + 1 week) procedures. Subjects who discontinue the study early between Day 28 and Day 49 should return to the study site within 48 hours to complete the EOS procedures.

[c] Significant medical history, including surgical history, will be obtained by consulting with the subject. Refer to Section 8.2 of protocol.

[d] RSV diagnostic testing determined in the 3 days before signing the ICF or at Screening may be used to assess eligibility. Subjects who were not tested for RSV as standard of care in the 3 days before signing the ICF may consent to the study and be tested for RSV during the Screening visit.

[e] If available, chest imaging obtained within 2 days before signing the ICF may be used to determine eligibility. If chest imaging is not available or was not obtained during standard care within 2 days before signing the ICF, a chest image (chest x-ray and/or tomography) must be obtained at Screening.

[f] Vital signs include heart rate, respiratory rate, systolic and diastolic blood pressure, and body temperature. Vital signs will be measured after the subject has been supine for a minimum of 5 minutes. For pulse oximetry assessments, record oxygen support level if not done on room air.

[g] If Screening and randomization/first dose occur on the same day (Day 1), then vital signs and pulse oximetry measured at Screening will be used as baseline values. If Screening (Day -1) and randomization/first dose (Day 1) occur on different calendar days within a 24-hour period, then vital signs and pulse oximetry will be performed again on Day 1 predose.

[h] A physical examination will be performed at Screening. Any subsequent physical examinations performed at the discretion of the Investigator will be targeted to new signs and symptoms including specific assessments of any changes from previous status.

[i] The physical examination performed at Screening will be used as the baseline assessment. If Screening (Day -1) and Randomization/first dose (Day 1) occur on different calendar days within a 24-hour period, a subsequent physical examination will not be required unless it is deemed necessary by the Investigator due to new signs and symptoms or for specific assessments of changes from previous status.

[j] Safety laboratory tests include chemistry, hematology, and urinalysis. Existing values collected in the 3 days before signing the ICF or at Screening may be used to assess eligibility.

[k] Although prior local safety laboratory test results may have been used to determine eligibility, separate safety laboratory samples must be collected before first dose and sent to the central laboratory for baseline assessment at Day 1.

[l] Height will be documented at Screening only. The BMI will be calculated at Screening (to assess eligibility) and other visits according to the following equation: BMI = (weight in kg)/(height in m^2).

[m] Pregnancy testing will be performed in female subjects of childbearing potential. A urine pregnancy test will be performed at Screening, Day 28, and at the EOS visit. In addition, on Day 1, blood will be collected for a serum pregnancy test to be performed by the central laboratory. The screening urine pregnancy test results will be used to qualify subjects at study entry. Refer to Section 8.4.2 of the protocol for pregnancy testing requirements for postmenopausal females.

[n] FSH should be tested in postmenopausal females. Refer to Section 8.4.2 of the protocol.

[o] Subjects who meet all inclusion criteria and none of the exclusion criteria will be eligible to enter the study and will be randomized 2:1 to receive 800 mg of EDP-938 or placebo. Subject randomization will be stratified by ribavirin treatment (presence or absence) and absolute lymphocyte count (<200 or ≥200 cells/µL) at Screening.

[redacted]

[q] Two nasal/nasopharyngeal swabs, one from each nostril, will be collected predose at each visit. Residual sample from nasopharyngeal swab collection may be stored for exploratory biomarker assessments.

[r] Subject participation is optional. Subjects will be required to review and sign a separate ICF for this assessment. Day 1 and 21 samples should be collected predose.

[s] Study drug (EDP-938 or placebo) should be administered during the study visit on days when clinic visits occur. Study visits should be scheduled close to the time that the subject normally takes the study drug so that dosing can occur during the visit. See Section 5.7 of the protocol for additional dosing details.

[t] Subjects should bring their study drug with them as part of their study site visit for drug accountability and for dosing of study drug. Study drug accountability will occur through a tablet count at each visit during Treatment and up through the Day 21 EOT visit.

[u] On Day 1, Day 7, and Day 21, two samples will be collected: one predose, collected within 1 hour before dosing (preferably within 30 minutes of dosing if possible) and at the same approximate time as that of the nasopharyngeal swab collection and one postdose, collected 1-3 hours postdose. At all other visits, one predose plasma PK sample will be collected at the same approximate time as that of the nasopharyngeal swab collection. Time and date of collection should be recorded in source and in the eCRF. Subjects who discontinue treatment early (before completing 21 days of dosing) should return to the study site within 24 hours after the last dose of study treatment to complete an EOT visit. One plasma PK sample will be collected at the same approximate time as that of the nasopharyngeal swab collection.

[v] For subjects taking CNI and/or mTOR inhibitor, a blood sample will be collected to be analyzed at the local laboratory for CNI and/or mTOR inhibitor blood levels and a separate sample will be collected for analysis at the central laboratory.

[w] Standard of care test results may include chest imaging reports, laboratory tests, electrocardiogram, or other assessments.

[x] Prior therapies will include medications and other therapies (including surgeries and other interventions) that end prior to the first dose of study drug. Concomitant therapies will include medications and other therapies (including surgeries and other interventions) ongoing at the first dose of study drug or started any time after the first dose of study drug. Any medication or therapy (including surgeries and other interventions) taken within 1 month of signing the ICF (Screening) and during the study through the end of the study will be recorded.

Signature

	Name	Function	Date	Signature
Written and Approved by*	[redacted]			

	Name	Function
Reviewed by	[redacted]	

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