# Statistical Analysis Plan

# Ridgeback Biotherapeutics LP

# EIDD-2801-2004

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# Glossary of Abbreviations

| Abbreviation | Term |
|---|---|
| AE | Adverse event |
| ALT | Alanine aminotransferase |
| ANCOVA | Analysis of covariance |
| AST | Aspartate aminotransferase |
| ATC | Anatomical therapeutic chemical |
| AUC | Area under the curve |
| $AUC_t$ | Area under the plasma concentration-time curve from time zero to time t |
| BID | Bis in die (Twice a day) |
| BMI | Body mass index |
| CBC | Complete blood count |
| $C_t$ | Plasma drug concentration at a specified time t after the administration of a given dose |
| CI | Confidence interval |
| $C_{max}$ | Maximum concentration |
| CMP | Comprehensive metabolic panels |
| CoV | Coronavirus |
| COVID-19 | Coronavirus Disease – 2019 |
| CRF | Case report form |
| DAIDS | Division of acquired immune deficiency syndrome |
| DB | Double-blind |
| EAS | Evaluable analysis set |
| ECG | Electrocardiogram |
| eCRF | Electronic case report forms |
| Hgb | Hemoglobin |
| ICU | Intensive care unit |
| IL-6 | Interleukin 6 |
| ITT | Intention-to-treat |
| LOD | Limit of detection |
| MAR | Missing at random |
| MCAR | Missing completely at random |
| MedDRA | Medical dictionary for regulatory activities |
| MMRM | Mixed model for repeated measures |
| NHC | $N^4$-Hydroxycytidine |
| NHC-TP | 5′-triphosphate metabolite of NHC |
| NP | Nasopharyngeal |
| PBMC | Peripheral blood mononuclear cells |
| PCR | Polymerase chain reaction |
| PK | Pharmacokinetic |
| PPS | Per-protocol set |
| PT | Preferred term |
| qPCR | Quantitative polymerase chain reaction |
| QTc | Corrected QT |
| RNA | Ribonucleic acid |
| SAE | Serious adverse event |
| SAP | Statistical analysis plan |
| SARS-CoV-2 | Severe acute respiratory syndrome coronavirus 2 |

| | |
|---|---|
| SD | Standard deviation |
| SI | International system of units |
| SOC | System organ class |
| SNP | Single-nucleotide polymorphism |
| SRC | Safety review committee |
| TFLs | Tables, figures and listings |
| ULN | Upper limit of normal |
| WHO | World health organization |

# STATISTICAL ANALYSIS PLAN AMENDMENT 1

The statistical analysis plan has been updated to reflect the changes in the protocol from v3.2 to v5.0. These include:

- An increase in the total sample size from 60 up to 80
- 3 additional dose groups at dose levels of 400mg, 800mg and an optional third group in part 4, at a dose level to be determined
- The 200mg dose level will be discontinued
- Clarification of the sequence of enrollment for each study part
- The secondary virological endpoint for measurement of the decline in viral RNA was revised to include endpoints corresponding to each of the planned sampling timepoints
- Secondary clinical endpoint #1 was modified to remove convalescent plasma
- Exploratory viral endpoints related to nasal swabs, saliva, and stool samples have been removed
- Removal of stratification by intention to use remdesivir in the randomization
- Removal of prolonged QTc to ≥500 msec was deleted, as this parameter is not being collected

# STATISTICAL ANALYSIS PLAN AMENDMENT 2

Minor amendment from SAP v2.0 to SAP v2.1 to clarify details which include:

- Categorization of age and BMI
- Definition of baseline
- Definition for how the onset of COVID-19 symptoms is to be determined
- Removal of screen failure table, since this is not collected
- Definition of antiviral medication
- Addition of imputation rules for concomitant medication dates

# STATISTICAL ANALYSIS PLAN AMENDMENT 3

Amendments from SAP v2.1 to SAP v3.0 to clarify details which include:

- Update to versioning of TFLs to be consistent with the SAP
- Visit window updates in Section 5.1
- Imputation of infectivity assay added to Section 5.2
- Additional covariates added to Section 6.5.2.2 and 6.5.2.3
- Baseline summary added to Section 6.5.4.1
- COVID-19 Risk group updated in Section 6.5.3 with the addition of a new table
- New table added for undetectable infections vital RNA in Section 6.5.4.1

# 1. Source Documents

The Statistical Analysis Plan (SAP) was written based on the following documentation:

| Document | Date | Version |
|---|---|---|
| Protocol | 11 March 2021 | 6.0 |
| eCRF | 27-Aug-2020 | 1.0 |

# 2. Protocol Details

## 2.1 Study Objectives

- Primary:
    1. To test whether orally administered EIDD-2801 results in a greater proportion of clearance from nasopharyngeal (NP) swabs compared to placebo in hospitalized adults by achieving undetectable (below the limit of detection [LOD] of the assay) viral RNA by day 5 after initiation of study drug.
    2. To evaluate the safety of treatment with EIDD-2801 in participants diagnosed with COVID-19.
- Secondary:
    1. To evaluate the efficacy of EIDD-2801 on clearance of SARS-CoV-2 RNA.
    2. To evaluate the effect of EIDD-2801 on improvement of clinical symptoms and signs of COVID-19.
    3. To evaluate EIDD-1931 pharmacokinetics in plasma in a subset of participants.
- Exploratory:
    1. To evaluate the efficacy of EIDD-2801 to clear SARS-CoV-2 RNA and infectious virus.
    2. To ascertain the role of EIDD-2801 in improvement of clinical symptoms and signs of COVID-19.
    3. To characterize the pharmacokinetics of EIDD-2061 (NHC-TP) in peripheral blood mononuclear cells (PBMC) in a subset of participants.

## 2.2 Overall Study Design

This study is a phase 2a randomized, placebo-controlled, double-blinded clinical trial of EIDD-2801 in adult men and women who have tested positive for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection by polymerase chain reaction (PCR) test within 6 days (144 hours) prior to randomization and are hospitalized with a diagnosis of COVID-19. Rapid enrollment and treatment will be initiated such that the first dose of EIDD-2801 or placebo will be administered as soon as possible and within 8 days of onset of symptoms.

Participants will be enrolled in up to 4 sequential study parts. During Part 1, participants will be randomized in a 1:1:1 ratio to:200 mg EIDD-2801:400 mg EIDD-2801: placebo. In Part 2 of the study, 21 participants will be randomized in a 2:1 ratio to receive EIDD-2801 400 mg or placebo and in Part 3 of the study, 21 participants will be randomized in a 2:1 ratio to receive EIDD-2801 800 mg or placebo. An optional Part 4 may be added during which 21 participants will be randomized in a 2:1 to EIDD-2801: placebo and the dose of EIDD-2801 may be the same or lower than doses studied in previous Part(s), but not to exceed 800mg bis in die (BID, twice a day). In v2.0 of the protocol, participants were randomized in a 1:1:1 ratio to 200 mg EIDD-2801:300 mg EIDD-2801: placebo. The EIDD-2801 300 mg arm was replaced with EIDD-2801 400 mg in v3.0 of the protocol.

The study parts will be conducted in sequence as follows: Enrollment into Part 1 of the study may be terminated upon approval and implementation of Protocol Amendment 3, and enrollment into Part 2 will be initiated immediately thereafter. Enrollment into Part 3 will be initiated once Part 2 has been fully enrolled. If initiated, Part 4 may begin enrolling participants as soon as Part 3 has been fully enrolled. Study parts 2 and 3 may be terminated prematurely based on emerging data from this and other ongoing studies of EIDD-2801.

EIDD2801 (100- and 200-mg capsules) and matching placebo will be supplied as dry filled capsules for oral administration. Doses of EIDD-2801 or matching placebo will be administered as combinations of 100- and 200-mg capsules in such a way as to preserve the study blind and as appropriate for the dose level. Participants will be administered study drug BID for 5 days (10 doses). In the event of missed doses, if the total number of missed doses is 4 or fewer, the number of days of study drug can be extended by no more than one day (through day 6) with the equivalent of missed doses up to 2 doses. If the participant misses more than 4 consecutive doses, or more than 5 total doses, then the participant will be discontinued from any further study drug administration and followed for safety for the remainder of the study.

The study is comprised of 3 periods: screening period, treatment period, and follow-up period. The screening period may last up to 2 days. The treatment period is 5 days of dosing with study drug. The follow-up period is 23 days and continues to at least day 28. For inpatients, clinical assessments will occur on days 3, 5, 8, 11, 15, 19, and 28. PK assessments will initiate on day 3 for participants who are still inpatients and be collected up to 24 hours' post-day 3 on day 4 where possible. For patients who are discharged (outpatients), clinical assessments will occur on days 3, 5, 8, 11, and 28 with a telephone assessment on day 15 (±1).

Interim analyses will be conducted after 25% and 50% of randomized participants reach day 14 after the initiation of study drug. No formal stopping rule is specified. Blinded data will be reviewed by the principal investigators and the sponsor, further details are provided in section 6.7.

## 2.3 Sample Size and Power

Because of the multiple arm design (placebo versus multiple doses of EIDD-2801), the power calculations are based on an individual dose arm versus placebo comparison, using a Fisher's exact test. Participants receiving the same doses across

study parts will be pooled together in the final analysis. It is expected that 14 or more participants will receive EIDD-2801 in the higher dose groups, and at least 14 participants will receive placebo across the study parts. Based on previous data (Wolfel, Nature, 2020), it is conservatively assumed that 20% of placebo recipients (n=20) will have clearance, i.e., undetectable SARS-CoV-2 RNA at day 5, compared to 80% clearance in an EIDD-2801 arm (n=20). This will provide83% power to detect a difference with α=0.05.

## 2.4 Randomization

To allow non-Johns Hopkins University sites to enroll, the randomization list is further stratified by site. To prevent incomplete blocks per site and unequal randomization, each site must completely enroll all assigned blocks of 6. Upon the overall recruitment target being met the overall number and allocation of study drug arms will be reviewed to determine if a significant random imbalance in the allocation of study drugs has occurred which would impact the power of the study. Depending upon the balance of screening failures by study drug arm, it is anticipated that randomization will continue to allow for up to 80 participants in the efficacy analysis set (EAS).

# 3. Efficacy and Safety Variables

## 3.1 Primary Efficacy Endpoint

- Achievement of undetectable (below the limit of detection of the assay) SARS-CoV-2 RNA by day 5 in NP swabs by quantitative Polymerase Chain Reaction (qPCR).

## 3.2 Secondary Efficacy Endpoints

- Time to clearance of viral RNA in NP swabs by qPCR.
- The decline in viral RNA copies/mL by days 3, 5, 8, 11, 15, and 19after initiation of study drug in NP swabs by qPCR.
- The rate of decline in viral RNA (change in log10 viral RNA copies/mL per day) in NP swabs by qPCR.

## 3.3 Exploratory Efficacy Endpoints

- Achievement of undetectable (below the LOD of the assay) viral titers by day 5 in NP swabs by infectivity assay.
- Time to clearance of infectious virus in NP swabs by infectivity assay.
- Clearance of infectious virus by day 3 and day 5 in NP swabs by infectivity assay.
- The number of acquired single-nucleotide polymorphisms (SNPs) in SARS-CoV-2 genomes by day 5 or day 11 in NP swabs by viral sequencing.

## 3.4 Primary Safety Endpoints

1. Adverse events (AEs)

2. Serious adverse events (SAEs)
3. Physical examination including vital signs
4. Safety laboratory assessments:
    a. complete blood counts (CBC) with differentials
        i. decrease in hemoglobin (Hgb) by >1 g/dL, or to <9 g/dL
        ii. decrease in platelet count by 50,000/µL, or to <75,000/µL
    b. comprehensive metabolic panels (CMP) including liver function tests
        i. increase in aspartate aminotransferase (AST), alanine aminotransferase (ALT), amylase, or lipase to ≥3xthe upper limit of normal (ULN)
    c. urinalysis
5. Electrocardiograms (ECGs)

## 3.5 Secondary Clinical Endpoints

1. Peak stage on the World Health Organization (WHO) Ordinal Scale for Clinical Improvement OR clinical requirement for addition of other therapeutics including but not limited to:
    - PEGylated interferon alpha
    - Inhaled interferon beta1
    - Ribavirin (any formulation)
    - Any interleukin (IL)-6 inhibitor
2. Number of days of supplemental oxygen
3. Number of days of mechanical ventilation
4. Number of days in the Intensive Care Unit (ICU)
5. Death

## 3.6 Exploratory Clinical Endpoints

1. Days of hospitalization
2. Time to resolution of COVID-19 symptoms defined as:
    - Fevers OR
    - At least one of the following symptoms: cough, shortness of breath, respiratory rate ≥20, radiographic evidence of pneumonia OR
    - other clinical symptoms or signs of pneumonia that are not otherwise explained by comorbidities or co-diagnoses
3. Number of days until a 2-point decrease in stage according to the WHO Ordinal Scale for Clinical Improvement.
4. Radiologic improvement by grading chest diagnostics (when radiography is available)

5. Change in IL-6 levels by day 5

## 3.7 Pharmacokinetic Endpoints

In Plasma:

1. Maximum EIDD-1931 concentration ($C_{max}$)
2. 1.5-hour EIDD-1931 concentration ($C_{1.5}$)
3. 3-hour EIDD-1931 concentration ($C_3$)
4. Area under the concentration: time curve of EIDD-1931 ($AUC_{0-8}$)
5. Elimination half-life ($t_{1/2}$) of EIDD-1931

(EIDD-1931 is the primary circulating form of EIDD-2801 in plasma)

# 4. Analysis populations

## 4.1 Screened

All participants who consent to participate and who undergo screening will be included in the screened population.

## 4.2 Randomized

All participants who consent to participate and who are randomized will be included in the randomized population.

## 4.3 Safety

All participants treated with at least one dose of study drug will be included in the Safety population. Safety participants are analyzed according to their actual treatment received. Participants who received EIDD-2801 300mg will be analyzed in the 200mg study group in all analyses using the safety population.

## 4.4 Intent-to-treat Set

The Intent-to-treat set (ITT) will consist of all randomized participants consistent with v5.0 of the protocol. ITT participants are analyzed according to their randomized treatment. Participants originally allocated to EIDD-2801 300mg will be analyzed in the 200mg study group in all analyses using the ITT population.

## 4.5 Efficacy Analysis Set

The Efficacy Analysis Set (EAS) will consist of all participants treated with at least one dose of study drug and with at least 1 post baseline assessment of SARS-CoV-2 RNA in NP swabs by qPCR. Efficacy analysis set participants are analyzed according to their actual treatment received. Participants who received EIDD-2801 300mg will be analyzed in the 200mg study group in all analyses using the EAS population.

## 4.6 Per Protocol Set

The Per-Protocol Set (PPS) will consist of all participants in the ITT population who do not have any important protocol deviations leading to exclusion from the PPS.

Protocol deviations are defined as any change, divergence, or departure from the study design or procedures defined in the study protocol. Important protocol deviations are a subset of protocol deviations that may significantly impact the correctness, accuracy, and/or reliability of the study data or that may significantly affect a subject's rights, safety, or well-being. Section 4.6.1 details important protocol deviations.

### 4.6.1 Important Protocol Deviations Potentially Leading to Exclusion from the PPS Analysis

Only those important protocol deviations considered to have a major effect on efficacy will lead to exclusion of the participants from the PPS. For the purposes of this study, the following criteria have been identified as potentially important protocol deviations, as it is considered that the occurrences of any of these criteria might have an important influence on the primary efficacy endpoint. Participants will be assessed purely by comparison of their electronic case report form (eCRF) data with the criteria below; protocol waivers will not be taken into consideration.

| Type | Important Protocol Deviation | Method of Identification |
|---|---|---|
| Inclusion/Exclusion Criteria Violation | Any violation of inclusion/exclusion criteria as specified in section 3.1 and 3.2 of the protocol . | Violations will be identified through site monitoring and entered into the deviation log. |
| Prohibited Medication | Prohibited medications identified in section 4.7 of the protocol include any other nucleos(t)ide analog drugs | Identified using the concomitant medications eCRF. |
| Minimum exposure to study treatment | Any participant who misses more than 4 consecutive doses, or more than 5 total doses. | Identified using the study drug administration eCRF. |
| Visit compliance | Any participant where the day 5 visit occurs more than 24 hours from the scheduled visit date. | Identified using the virologic sampling eCRF. |
| Unblinding | Any participant whose treatment allocation is accidentally unblinded or unblinded as part of an emergency because of safety concerns. | Identified through reports of protocol deviation or records of emergency unblinding. |

All-important protocol deviations, potentially leading to exclusion from the PPS, will be reviewed and approved by Ridgeback Biotherapeutics LP prior to database lock and unblinding. Should additional important protocol deviations leading to exclusion from the PPS not anticipated at the time of preparing this SAP be identified during

the study and prior to unblinding, they will be documented in a SAP amendment and included in all relevant protocol deviation reviews and approvals.

## 4.7 Pharmacokinetic

All participants treated with at least one dose of study drug with at least one reportable concentration of EIDD-1931 will be included in the plasma pharmacokinetic (PK) population and their data included in the plasma population PK dataset. Participants will be considered evaluable for the formal PK endpoints if specimens were collected for protocol-specified time points necessary to define those endpoints.

# 5. DataHandling

## 5.1 Time points and Visit Windows

Day 1 is defined as the day of first dose of study drug. Relative days after day 1 are calculated as (assessment date – day 1 date) + 1. Relative days prior to day 1 are calculated as (assessment date – day 1 date). The day prior to day 1 is day -1.

For all populations, all other assessments will be assigned to visits as follows:

- Assessments with missing data and assessments marked "Not Done" will be considered as providing a missing response and are not permitted to be assigned to a visit window.
- If multiple measurements are available within a visit window then the closest measurement taken to the scheduled day of visit will be used. If two measurements are equidistant to the scheduled day of visit then the latest measurement will be used (e.g. if measurements are available for day 4 and 6 then day 6 will be used for day 5 analysis measurement)

For virologic endpoints (NP swabs, BAL and/or sputum), clinical endpoints (WHO ordinal scale and clinical assessments) and safety endpoints of AE/SAE reporting, vital signs, pulse oximetry, full physical examination and chest radiography the following visit windows will be applied:

| Visit | Scheduled Day of Visit | Visit Window |
|---|---|---|
| Screening | Nominal visit | NA |
| Day 1 | 1 | 1 |
| Day 3 | 3 | 2 to 3 |
| Day 5 | 5 | 4 to 6 |
| Day 8 | 8 | 7 to 9 |
| Day 11 | 11 | 10 to 13 |
| Day 15 | 15 | 14 to 17 |
| Day 19 | 19 | 18 to 24 |
| Day 28 | 29 | ≥25 |
| Early Discontinuation | Nominal visit | NA |

For laboratory assessments the following visit windows will be applied:

| Visit | Scheduled Day of Visit | Visit Window |
|---|---|---|
| Screening | Nominal visit | NA |
| Day 1 | 1 | 1 |
| Day 3 | 3 | 2 to 3 |
| Day 5 | 5 | 4 to 6 |
| Day 8 | 8 | 7 to 11 |
| Day 15 | 15 | 12 to 17 |
| Day 19 | 19 | ≥18 |
| Early Discontinuation | Nominal visit | NA |

For targeted physical examination the following visit windows will be applied:

| Visit | Scheduled Day of Visit | Visit Window |
|---|---|---|
| Screening | Nominal visit | NA |
| Day 1 | 1 | 1 |
| Day 3 | 3 | 2 to 3 |
| Day 5 | 5 | 4 to 6 |
| Day 8 | 8 | 7 to 9 |
| Day 11 | 11 | 10 to 13 |
| Day 15 | 15 | 14 to 17 |
| Day 19 | 19 | ≥18 |
| Early Discontinuation | Nominal visit | NA |

12-lead ECG measurements will not be assigned a visit and are analyzed as baseline or post-baseline only.

## 5.2 Handling of Dropouts, Missing Data, and Outliers

Participants who prematurely discontinue from the study without receiving a single dose of study drug or placebo will be replaced. Participants who prematurely discontinue should undergo an end of study visit at day 28 to evaluate clinical assessments, AEs and SAEs.

For the analysis of the primary efficacy endpoint, if a participant's NP swab at day 5 is not available for analysis then a participant's response will be imputed to have a detectable level of SARS-CoV-2 RNA by qPCR (non-response). For participants enrolled prior to protocol v5.0, both NP swabs need to be unavailable for a participant's response to be imputed as a detectable level of SARS-CoV-2 RNA by qPCR (non-response). Longitudinal analyses of secondary endpoints, such as the rate of decline of log10 viral RNA copies/mL in NP swabs, will use mixed effect models (described in Section 6.5.2) which are robust for missing data when this is missing completely at random (MCAR) or missing at random (MAR). Time to event analyses of secondary endpoints, such as the time to clearance of viral RNA in NP swabs, will use Kaplan-Meier analyses which will censor participants who are lost to follow-up with no measurements available at their last available assessment.

For the analysis of the exploratory efficacy endpoints, analyzing infectivity assay data, subjects with missing infectivity data will be imputed based on the rules provided in the following table.

| **Visit Before** | **Visit After** | **Imputed Infectivity Result** |
|---|---|---|
| Negative | Negative | Negative |
| Positive | Positive | Positive |
| Negative or missing | Positive | Positive* |
| Missing | Negative | Missing |
| Any Value | Missing | Missing |

* Subjects with missing baseline and reported the first post baseline value of positive, the baseline will be imputed as positive.

Missing safety data will generally not be imputed. However, safety assessment values of the form of "<x" (i.e. below the lower limit of quantification) or ">x" (i.e. above the upper limit of quantification) will be imputed as "x" in the calculation of summary statistics but displayed as "<x" or ">x" in the listings. Additionally, AEs that have missing causality (after data querying) will be assumed to be related to study drug.

For missing start AE and concomitant medication dates, the following will be applied:

- Missing day – impute the 1st of the month unless month is same as month of first dose of study drug then impute first dose date.
- Missing day and month – impute 1st January unless year is the same as first dose date then impute first dose date.
- Completely missing – impute first dose date unless the end date suggests it could have started prior to this in which case impute the 1st January of the same year as the end date.

Note: When imputing a start date, ensure that the new imputed date is sensible i.e. is prior to the end date of the AE or treatment.

For missing end AE and concomitant medication dates, the following will be applied:

- Missing day – impute the last day of the month unless month is the same as month of scheduled end of study visit (day 28) then impute scheduled end of study visit (day 28).

Missing day and month – impute 31st December unless year is the same as scheduled end of study visit (day 28) then impute scheduled end of study visit (day 28). No imputation of AE grade will occur for AEs missing DAIDS grade.

No rules for outlier detection are planned.

# 6. Statistical Methods

## 6.1 General Principles

All data processing, summarization and analyses will be performed using statistical software package.

Unless specified, participants receiving or assigned the same treatment across parts of the study will be pooled in all analyses e.g., presentations of the placebo study group will include participants from parts 1-4. Safety endpoints will be presented for all study groups.

Listings of virological endpoints will include all sample collection methods.

For SARS-CoV-2 RNA values reported as below the lower limit of quantification (<1018), the lower value (1017) will be used in the analyses.

Baseline is defined as the last scheduled assessment collected prior to the first dose of the study drug except where otherwise indicated. For assessments on the same date as the first dose of study drug, but where assessment time is missing, the assessment will be presumed to take place prior to the first dose of study drug and used as a baseline assessment.

The following principles will be applied to all tables, figures and listings (TFLs) unless otherwise stated:

| Principle | Value |
|---|---|
| Significant tests | Two-sided and use a 5% significance level for main effects and 5% significance level for interaction terms. |
| Treatment group labels and order presented | Placebo<br>200mg EIDD-2801<br>EIDD-2801 (listings only)<br>400mg EIDD-2801<br>800mg EIDD-2801<br><Part 4 TBD> EIDD-2801<br>For baseline and demographic tables: All Participants<br>For efficacy tables: All EIDD-2801 |
| Tables | Data in summary tables will be presented by study group, assessment and visit (where applicable). |
| Listings | All data collected presented by study group, participant, assessment and visit (where applicable), unless otherwise specified. |
| Descriptive summary statistics for continuous variables | Number of participants/observations (N), mean, standard deviation (SD), median and range. |
| Descriptive summary statistics for categorical variables | Frequency counts and percentages [n (%)] |
| Denominator for percentages | Number of participants in the analysis population, unless stated otherwise in table shell(s). |
| Include "Missing" as category | Yes, when the number missing is greater than zero for at least one study group. |
| Display for 0 percentages | Blank |

| Principle | Value |
|---|---|
| Display to one more decimal place than collected value | Mean<br>Standard Error<br>Mean Difference<br>Median |
| Display to two more decimal places than collected value | Standard Deviation<br>Confidence Interval |
| Limit of precision for displays | 3 significant figures<br>If minimum is ≥100% display to 0 decimal places<br>If reported as x.xxx, display to 3 decimal places |
| Date Format | DDMMMYYYY |
| Source footnotes | Each table will have a footnote that lists the source data listing(s). Each figure will have a footnote that list the source table(s). |
| Dictionary names and versions | The dictionary names and versions will be included in a footnote in all AE and prior or concomitant medication TFLs that present coded terms from the dictionaries. |

## 6.2 Subject Disposition and Data Sets Analyzed

Participant disposition will be listed and summarized by study group and overall. Furthermore, a summary for each study part and overall will be presented. Patient disposition will include the number and percentage of participants:

- screened;
- randomized;
- randomized and not treated;
- treated;
- included in each study population (Safety, ITT, EAS, PPS, PK).

In addition, the number and percentage of participants who complete treatment (defined as ≥10 doses) and who discontinue early (missed more than 4 consecutive doses or more than 5 total doses.) will be presented. Furthermore, for subjects who do not complete the study, the primary reason for not completing the study will be presented.

A summary of participant enrollment by site will also be provided by study group and overall for the safety population.

## 6.3 Protocol Deviations

All protocol deviations will be listed and summarized by study group for the ITT population.

All-important protocol deviations leading to exclusion from the PPS population (see Section 4.6.1 will be listed and summarized by study group for the ITT population.

The deviations will be identified before data are unblinded.

## 6.4 Demographics and Other Baseline Characteristics

Demographic and important baseline characteristics will be listed and summarized by study group and overall for the Safety and ITT Populations. Furthermore, a summary for each study part and overall will be presented for the safety and ITT populations. Standard descriptive statistics will be presented for the continuous variables of:

- age (years);
- weight (kg);
- height (cm);
- body mass index (BMI) (kg/$m^2$) (categories: <25, ≥25 to <30, and ≥30)
- baseline viral RNA (log10 copies/mL)
- baseline Peripheral Capillary Oxygen Saturation (SpO2)
- baseline Systolic blood pressure (mmHg)
- baseline Diastolic blood pressure (mmHg)
- baseline pulse rate (beats/min)
- baseline body temperature (ºC)
- baseline respiratory rate (breaths/min)
- days from onset of symptoms to first dose (defined as the date of first dose – date of symptom onset + 1, where date of symptom onset is the earliest date collected in medical history where "COVID-related" is recorded)

The total counts and percentages of participants will be presented for the categorical variables of:

- age group (years) (grouped as <40, ≥40 to <65 and ≥65);
- use of remdesivir as a concomitant medication
- sex;
- race;
- ethnicity;
- baseline WHO ordinal scale for clinical improvement

No formal tests of statistical significance will be performed on the demographic and baseline data (if no inferential tests are planned).

Other baseline measurements, such as laboratory measurements, will be summarized by study group with the post-baseline measurements.

### 6.4.1 Medical History

Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 23.1 (or a later version if updated during the study). All medical history will be listed, and the number and percentage of participants with any medical

history will be summarized for the Safety Population by system organ class (SOC) and preferred term (PT) for each study group and overall.

### 6.4.2 Previous and Concomitant Medications

Medications received prior to or concomitantly with study drug will be coded by using the WHODrug Dictionary Version March 2019 Global Dictionary Version B3 (or a later version if updated during the study), Anatomical Therapeutic Chemical (ATC) Classification codes. Additional antivirals including, but not limited to, PEGylated interferon alpha, inhaled interferon beta1, ribavirin (any formulation) and any interleukin (IL)-6 inhibitor will be flagged.

Prior medications and concomitant medications are defined as follows:

- Prior medications are those taken prior to study drug with a stop date prior to the first dose of study drug.
- Concomitant medications are those with a start date on or after the first dose date of study drug, or those with a start date before the first dose date of study drug and a stop date on or after the first dose date of study drug or ongoing end of study.

If a medication cannot be classified as "prior" or "concomitant" after applying imputation rules for missing/incomplete dates, it will be classified as concomitant.

Prior medications and concomitant medications will be listed together and summarized separately for the Safety population. Antiviral prior and concomitant medications will be identified in the listings using ATC-level 2 code J05.

The number and percentage of participants using each medication will be displayed together with the number and percentage of participants using at least one medication within each therapeutic class (ATC-Level 2), chemical subgroup (ATC-Level 4), and generic term.

## 6.5 Efficacy

### 6.5.1 Primary Efficacy Analysis

The response rate per study group will be calculated by the number of subjects below the LOD for SARS-CoV-2 RNA as measured using qPCR divided by the number of subjects randomized to that study group in the ITT population and will be presented along with 95% exact binomial confidence intervals for each study group. Each active dose group and the pooled EIDD-2801 group will be compared to the placebo group separately using the Fisher's Exact Test with a two-sided alpha level of 0.05. For subjects randomized prior to protocol v5.0, the response rate per study drug will be calculated using the number of subjects where both NP swabs at day 5 are below the limit of quantification for SARS-CoV-2 RNA as measured using qPCR for the numerator. If only one swab measurement is available, then this measurement will be used and if neither swab measurement is available participants will be imputed to have a value above the limit of quantification (non-response). If both measurements are available but the results are inconsistent then the participant will be considered to be above the limit of detectability.

## 6.5.2 Secondary Efficacy Analyses

### 6.5.2.1 Time to clearance of viral RNA in NP swabs

The time to clearance of viral RNA in NP swabs will not be formally assessed. The number and percentage of participants with detectable SARS-CoV-2 RNA in NP swabs as measured using qPCR will be presented for each visit in the schedule of assessments where NP swabs are collected. Furthermore, the change in viral RNA from baseline (log10 copies/mL) will be calculated as log10 viral RNA at visit – baseline viral RNA. For participants randomized prior to v5.0 where measurements of viral RNA are available from both baseline NP swabs, the average will be used. The number and percentage of subjects with a 1 log10 copies/mL, 2 log10 copies/mL and 3 log10 copies/mL decrease from baseline will be presented at each visit. Each active dose group and the pooled EIDD-2801 group will be compared to the placebo group separately using the Fisher's Exact Test with a two-sided alpha level of 0.05.

### 6.5.2.2 Rate of decline in viral RNA in NP swabs

The individual rate of SARS-CoV-2 RNA decline will be derived as Average Area Under the Curve Minus Baseline (AAUCMB) for the 0-3 days, 0-5 days, 0-8 days, and 0-11 days using the following formulas:

$$\mathrm{AUC} = \sum_{i=1}^{n-1} \left(t_{i+1} - t_i\right)\left(\frac{x_{i+1} + x_i}{2}\right),$$

$$\mathrm{AAUC} = \frac{\sum_{i=1}^{n-1} \left(t_{i+1} - t_i\right)\left(\frac{x_{i+1} + x_i}{2}\right)}{\left(t_n - t_1\right)} = \frac{\mathrm{AUC}}{\left(t_n - t_1\right)}, \text{ and}$$

AAUCMB=AAUC – Baseline (x at time i=1)

where, $x_i$ is the data value at the $i^{th}$ time point and $t_i$ is the time value at the $i^{th}$ time point.

The AAUCMB will be analyzed using an Analysis of Covariance (ANCOVA) model with terms for study group, days from onset of symptoms to first dose and baseline SARS-CoV-2 RNA by the time interval. The estimated treatment difference for "Active – Placebo" for each time interval will be displayed in the summary of statistical analysis together with the 95% confidence interval and the associated p-value. Least Squares Means will also be presented with the standard error.

### 6.5.2.3 Decline in viral RNA in NP swabs

The decline in log10 viral RNA copies/mL in NP swabs by qPCR will be calculated using a mixed effect model for repeated measures in the EAS population. The dependent variable will be log10 viral RNA copies/mL in NP swabs by qPCR, both swab measurements from a visit for a participant will be included if available. The independent fixed effect variables will include study drug (reference group will be placebo), days from first dose of study drug (day of NP swab-first dose of study drug

+1), baseline log10 viral RNA copies in NP swabs by qPCR, days from onset of symptoms to first dose, an interaction of days from onset of symptoms to first dose and visit, an interaction of baseline RNA and visit, and an interaction term between study drug and days from first dose of study drug (formal significance for the interaction term will be determined by $p<0.05$). A random intercept will be included per participant and an unstructured covariance matrix will be used, estimated using restricted maximum likelihood.

The statistical model estimated will be used to calculate the least squares mean (LSmean), treatment estimates, treatment differences (each active EIDD-2801 dose – placebo) and 95% CI at days 3, 5, 8, 11, 15(in patient only), 19 (in patient only) and 28 (outpatient only).

### 6.5.3 Subgroup Analysis

Exploratory analyses of the primary and secondary efficacy endpoints discussed in sections 6.5.1 and 6.5.2, as well as all safety endpoints for adverse events and laboratory assessments discussed in sections 6.6.2 and 6.6.3, will be performed for the following subgroups:

- Use of remdesivir as a concomitant medication (No use, use)
- COVID-19 risk group (0, 1, ≥2)

Note that for purposes of analyses the COVID-19 risk groups may be collapsed to 0 and ≥1, if the data warrants it.

A participant's COVID-19 risk group is defined based on the number of the below criteria applicable at baseline assessment:

- Cancer
- Chronic kidney disease
- COPD (chronic obstructive pulmonary disease)
- Down Syndrome
- Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies
- Immunocompromised state (weakened immune system) from solid organ transplant
- Currently receiving immunosuppressive treatment
- Obesity (body mass index [BMI] of 30 kg/m2 or higher but < 40 kg/m2)
- Body mass index of 35 or higher
- Are 65 years or older
- Are 55 years or older and have hypertension)
- Sickle cell disease
- Smoking (Current or former)
- Type 2 diabetes mellitus

Note that subjects assigned to the obesity (BMI of 30<- to <40) and the BMI of 35 or higher risk groups will be counted as 1 risk factor. Note, for the subgroup analysis by use of remdesivir the fixed terms for the use of remdesivir will be

removed from the models. The use of remdesivir as a concomitant medication will be determined using the rules defined in section 6.4.2.

### 6.5.4 Exploratory Efficacy Analysis

#### 6.5.4.1 Undetectable infectious viral RNA by day 3 and day 5 in NP swabs

Infectious viral RNA in NP swabs will be determined using an infectivity assay and will provide a binary indication if infectious viral RNA is present. The presence of infectious viral RNA at days 1, 3, 5, 8, 11, 15 (in patient only), 19 (in patient only) and 28 (outpatient only) will be analyzed using the same method as specified in section 6.5.1 for the primary efficacy endpoint in the EAS population. The analysis will be repeated for subjects with a positive infectious viral RNA at baseline. Participants without a result for viral RNA in NP swabs by infectivity assay will be presented as missing for a visit and no imputation will be applied.

### 6.5.5 Secondary Clinical Analyses

#### 6.5.5.1 Peak Stage of WHO Ordinal Scale for Clinical Improvement

The number and percentage of participants per peak stage on the WHO Ordinal Scale for Clinical Improvement will be presented by study drug group in the safety population. Peak stage will refer to the highest (worst) measured scale per participant recorded after baseline. For WHO Ordinal Scale, the baseline measurement will allow for measurements to be taken up to 4 hours after the first dose of study treatment.

#### 6.5.5.2 Requirement for additional antivirals

The number and proportion of participants receiving additional antivirals (including, but not limited to, PEGylated interferon alpha, inhaled interferon beta1, ribavirin (any formulation) and any interleukin (IL)-6 inhibitor) after baseline will be presented per study drug group in the safety population along with the two-sided 95% CI using the Clopper-Pearson method (exact CI for a binomial proportion).

#### 6.5.5.3 Number of days of supplemental oxygen

The number of total days of supplemental oxygen is calculated per participant. This will be summarized continuously by study group. Participants who remain on supplemental oxygen at the end of study visit will have their value imputed as number of days of supplemental oxygen+1. Participants who require no supplemental oxygen will be analyzed with a value of 0. The peak amount of oxygen used will be summarized descriptively where available. These analyses will use the safety population.

#### 6.5.5.4 Number of days of mechanical ventilation

The number of total days of mechanical ventilation is calculated per participant. This will be summarized continuously by study group. Participants who remain on mechanical ventilation at the end of study visit will have their value imputed as number of days of mechanical ventilation+1. Participants who require no mechanical

ventilation will be analyzed with a value of 0. This analysis will use the safety population.

#### 6.5.5.5 Number of days in the ICU

The number of total days in the intensive care unit (ICU) is calculated per participant. This will be summarized continuously by study group. Participants who remain in the ICU at the end of study visit will have their value imputed as number of days in the ICU+1. Participants who no require ICU will be analyzed with a value of 0. This analysis will use the safety population.

#### 6.5.5.6 Death

The number and proportion of participants who died will be presented by study group along with the two-sided 95% CI using the Clopper-Pearson method (exact CI for a binomial proportion) for the safety population.

### 6.5.6 Exploratory Clinical Analyses

#### 6.5.6.1 Number of days of hospitalization

The number of days of hospitalization is calculated as last day of the hospitalization/end of study – first day in ICU +1). Participants will be administratively censored at the end of study visit date if participants still require hospitalization. The median (95% CI) number of days of hospitalization will be presented by study drug using the Kaplan-Meier method for the safety population. This will be summarized continuously by study group. Participants who remain in hospital at the end of study visit will have their value imputed as number of days of hospitalization+1. This analysis will use the safety population.

#### 6.5.6.2 Time until on room air without requirement for supplemental oxygen

The time until on room air without requirement for supplemental oxygen is defined as the time from first use of supplemental oxygento the first date where supplemental oxygen is no longer required (date supplemental oxygen discontinued – date of first use of supplemental oxygen + 1).The median (95% CI) time until on room air without the requirement for supplemental oxygen will be presented by study group using the Kaplan-Meier method for the safety population excluding participants who do not require supplemental oxygen.

#### 6.5.6.3 Time to resolution of COVID-19 symptoms

The time to resolution of COVID-19 symptoms is defined as the time from first dose of study drug to the first date where COVID-19 symptoms have been completely resolved (date COVID-19 symptom free– date of randomization +1). Resolution of COVID-19 symptoms is defined as the complete resolution of symptoms including: fever, cough, shortness of breath, respiratory rate ≥ 20 breaths per minute and other clinical symptoms or signs that are not otherwise explained by comorbidities or co-diagnoses. COVID-19 symptoms will be collected on the medical history eCRF at baseline and adverse event form during the study with a check box indicating if the sign or symptom is COVID-19 related. All adverse events and medical history related to COVID-19 must be resolved for a participant to be declared COVID-19 symptom

free. The median (95% CI) time to resolution of COVID-19 symptoms will be presented by study drug using the Kaplan-Meier method for the safety population.

#### 6.5.6.4 Number of days until a 2-point decrease in WHO Clinical improvement scale

The time to a 2-point decrease in the WHO clinical improvement scale is defined as the time from first dose of study drug to the first date where a 2-point decrease is detected (date 2-point decrease – date of randomization +1). The median (95% CI) time to a 2-point decrease will be presented by study drug using the Kaplan-Meier method for the safety population.

#### 6.5.6.5 Radiological improvement

Radiological impression from available radiographic reports will be listed by study drug, participant and visit.

#### 6.5.6.6 Change in interleukin (IL)-6 levels

The change from baseline in IL-6 levels will be summarized by study drug group at day 5, 19 (inpatient only) and 28 (outpatient only) after randomization in the EAS population. An ANCOVA analysis will be conducted with dependent variables of IL-6 at day 5 and independent variables of baseline IL-6 and study drug. The LSmean, treatment estimates, treatment differences (each active EIDD-2801 dose – placebo) and 95% CI will be presented. Other cytokine/inflammatory biomarkers analyzed as part of this clinical endpoint will be analyzed as described above. All IL-6 and other cytokine/inflammatory biomarkers will be listed.

### 6.5.7 Pharmacokinetic Analyses

#### 6.5.7.1 Pharmacokinetic Analysis

PK parameters will be determined using non-compartmental methods in validated software program, Phoenix WinNonlin (Certara, Version 8.1 or higher).

The pharmacokinetic analysis and presentation for PBMC samples will be analyzed separately with analyses pre-specified in a separate analysis plan.

The following parameters will be calculated where possible from the plasma concentrations of EIDD-2801 and EIDD-1931:

| Parameter | Units[a] | Definition |
|---|---|---|
| $AUC_{0-8}$ | h*ng/mL | area under the plasma concentration-time curve during a dosing interval[b] |
| $C_{max}$ | ng/mL | maximum observed concentration |
| $C_{1.5}$ | ng/mL | concentration at 1.5 hours postdose |
| $C_3$ | ng/mL | concentration at 3 hours postdose |
| $t_{max}$ | h | time of the maximum observed concentration |
| $t_{last}$ | h | time of the last quantifiable concentration |

| | | |
|---|---|---|
| $t_{1/2}$ | h | apparent terminal elimination half-life |

[a] Units are based on concentration units (provided by bioanalytical lab) and dose units used in the study.
[b] AUC will be calculated using the linear trapezoidal rule for increasing concentrations and the logarithmic rule for decreasing concentrations (linear up/log down rule).

Additional pharmacokinetic parameters may be calculated where appropriate.

Pharmacokinetic analysis will, where possible, be carried out using actual blood sampling times postdose. If an actual time is missing, the sample concentration result will be treated as missing unless there is scientific justification to include the result using the nominal time.

Pharmacokinetic parameters will be derived where possible for all subjects. Data from subjects with incomplete profiles (missed blood draws, lost samples, samples unable to be quantified) may be used if PK parameters can be estimated using the remaining data points.

The following molecular weights (MW) will be used in calculations where required

EIDD-1931 259.22 g/mol

EIDD-2061 TBC g/mol

$C_{max}$, $t_{last}$ and $t_{max}$ will be obtained directly from the concentration-time profiles. If $C_{max}$ occurs at more than 1 timepoint, $t_{max}$ will be assigned to the first occurrence of $C_{max}$.

PBMC EIDD-2061 : plasma EIDD-1931 ratios will be calculated, adjusting for the difference in molecular weight as follows:

$$(Concentration_{EIDD\text{-}1931}/MW_{EIDD\text{-}1931})/(Concentration_{EIDD\text{-}2061}/MW_{EIDD\text{-}2061})$$

Ratios will not be calculated where the time difference between the plasma and PBMC sample actual times differs by more than 10%.

### 6.5.7.2 Criteria for the Calculation of Apparent Terminal Elimination Rate Constant and Half-Life

The start of the terminal elimination phase for each subject will be defined by visual inspection and generally will be the first point at which there is no systematic deviation from the log-linear decline in concentrations.

The apparent terminal elimination rate constant ($\lambda_z$) will only be calculated when a reliable estimate can be obtained using at least 3 data points, preferably not including $C_{max}$, and the adjusted coefficient for determination of exponential fit ($R^2$-adj) of the regression line is ≥0.7. Parameters requiring $\lambda_z$ in their calculation (e.g., $AUC_{0\text{-}12}$, $t_{1/2}$) will only be calculated if the $R^2$-adj value of the regression line is ≥0.7.

The following regression-related diagnostic PK parameters will be determined:

| Parameter | Units | Definition |
|---|---|---|
| $\lambda_z$ | 1/h | apparent terminal elimination rate constant |
| $\lambda_z$ Upper | h | end of exponential fit |
| $\lambda_z$ Lower | h | start of exponential fit |
| $\lambda_z$ N | Not applicable | number of data points included in the log-linear regression |
| $\lambda_z$ Span Ratio | Not applicable | time period over which $\lambda_z$ was determined as a ratio of $t_{1/2}$ |
| $R^2$-adj | Not applicable | adjusted coefficient for determination of exponential fit |

Where possible, the span of time used in the determination of $\lambda_z$ (i.e. the difference between $\lambda_z$ Upper and $\lambda_z$ Lower) should be ≥2 half-lives. If the $\lambda_z$ Span Ratio is <2, the robustness of the $t_{1/2}$ values will be discussed in the CSR.

#### 6.5.7.3 Criteria for Calculation and Reporting of Area Under the Concentration-time Curve

The minimum requirement for the calculation of AUC will be the inclusion of at least 3 consecutive concentrations above the lower limit of quantification. If there are only 3 consecutive concentrations, at least 1 should follow $C_{max}$.

#### 6.5.7.4 Criteria for Handling Below the Limit of Quantification or Missing Concentrations for Pharmacokinetic Analysis

Plasma concentration values that are below the limit of quantification (BLQ) will be set to a value of zero, with the following defined exceptions which will be set to missing:

- Any embedded BLQ value (between 2 quantifiable concentrations).
- BLQ values following the last quantifiable concentration in a profile.
- If an entire concentration-time profile is BLQ, it will be excluded from PK analysis.

Where 2 or more consecutive concentrations are BLQ at the end of a profile, the profile will be deemed to have terminated and any further quantifiable concentrations will be set to missing for the calculation of the PK parameters unless they are considered to be a true characteristic of the profile of the drug.

If a predose plasma concentration is missing, it may be set to zero by default.

#### 6.5.7.5 Treatment of Outliers in Pharmacokinetic Analysis

If a value is considered to be anomalous due to being inconsistent with the expected PK profile, it may be appropriate to exclude this point from the PK analysis. However, the exclusion of data must have strong justification and will be documented in the CSR.

Quantifiable pre-dose concentration values prior to the first dose will be considered anomalous and set to missing for the PK analysis.

#### 6.5.7.6 Presentation of Pharmacokinetic Data

If the actual time of sample collection deviates by greater than ±10% from the protocol scheduled time the concentration will be flagged for exclusion from summary tables and corresponding figures.

Individual concentrations that are deemed to be anomalous will be flagged in the listings and excluded from the summary statistics. Summary tables, arithmetic mean figures, overlaying individual figures, and individual figures by treatment and time post-dose will be provided for plasma PK concentrations. All figures will be produced on both linear and semi-logarithmic scales. Individual (separate and overlaying) figures will be plotted using actual sample times and will be based upon the safety analysis set. Arithmetic mean figures will be based upon the PK population.

Summary tables by study group will be provided for all plasma PK parameters, with the exception of diagnostic regression-related PK parameters, which will be listed but not summarized.

A listing of PK blood sample collection times as well as derived time deviations and all reportable concentrations will be presented for EIDD-1931 for all participants for the safety population.

Plasma concentrations will be summarized for the PK population for each time point using protocol scheduled times and appropriate descriptive statistics (i.e., n, n below LLOQ, geometric mean [gmean], geometric standard deviation [gSD], , geometric coefficient of variance expressed as a percentage [gCV%], arithmetic mean [mean], arithmetic SD [SD], coefficient of variance expressed as a percentage [CV%], median, minimum and maximum).

The gmean is calculated as exponential ($\mu$), where $\mu$ is the arithmetic mean calculated using log transformed data.

The gCV% is calculated as 100 x sqrt[exp($s^2$)-1], where s is the SD of the log-transformed data.

The gmean±gSD (gmean-gSD and gmean+gSD) are calculated as exp($\mu \pm s$).

Individual concentrations below the LLOQ of the bioanalytical assay will be reported as BLQ in the listings with the LLOQ defined in the footnotes of the relevant tables, figures and listings.

Individual plasma concentrations that are Not Reportable will be reported as NR and those that are missing willbe reported as NS (No Sample) in the listings.

Plasma concentrations that are BLQ, NR or NS will be handled as follows for the provision of the descriptive statistics.

- Any values reported as NR or NS will be excluded from the summary tables and corresponding figures.
- At a timepoint where less than or equal to 50% of the concentration values are BLQ, all BLQ values will be set to 0, and all descriptive statistics will be calculated accordingly.
- At a timepoint where more than half of the values are BLQ, the gmean, gmean+gSD, gmean-gSD, gCV%, mean, SD and CV% will be set to NC. The maximum value will be reported from the individual data, and the minimum and median will be set to BLQ.
- If all values are BLQ at a time point, no descriptive statistics will be calculated for that time point. The gmean, mean, minimum, median and maximum will be reported as BLQ and gmean±gSD, gCV%, SD and CV% as NC.

The number of values below LLOQ (n <LLOQ) will be reported for each time point together with the total number of collected values (n).

Three observations >LLOQ are required as a minimum for a plasma concentration to be summarized. Two values >LLOQ are presented as a minimum and maximum with the other summary statistics as NC.

Plasma concentrations that are BLQ will be handled as follows for display in figures:

- Arithmetic mean plots will use the same BLQ handling rules as for the summary statistics
- For individual plots and combined individual plots: BLQ values prior to the first quantifiable concentration in that profile will be set to zero (linear plots only); after the first quantifiable concentration of the profile any BLQ values will be set to missing.

All reportable PK parameters will be listed for EIDD-1931 for participants in the PK population.

Plasma PK parameters for EIDD-1931 will be summarized for the PK analysis set by drug group using the following descriptive statistics:

- $C_{max}$ $C_{1.5}$, $C_{3,}AUC_{(0-8)}$, $t_{max}$ and $t_{1/2}$will present n, gmean, gSD, gmean 95% CI, gCV (%), mean, SD, CV%, median, min and max.

For the calculation of summary statistics of PK parameters, all not reportable (NR) and not calculated (NC) values will be set to missing. Three reportable values are required as a minimum for a PK parameter to be summarized. Two values are presented as a minimum and maximum with the other summary statistics as NC. If

one or more values for a given parameter is zero (or imputed with zero), then no geometric statistics will be calculated for that parameter and the results for geometric statistics will be set to "NA", not applicable.

#### 6.5.7.7 Precision and Rounding Rules

PK concentration data will be presented in the listings to the same number of significant digits as the data received from the bioanalytical laboratory (usually to 3 significant figures) and against the same units as received.

PK concentration descriptive statistics will all be presented to 4 significant figures with the exception of the minimum and maximum which will be presented to 3 significant figures and n and n<LLOQ which will be presented as integers.

For plasma PK parameters, the listings will be presented according to the following rules:

- $C_{max}$, $C_{1.5}$, $C_3$– will be presented to the same number of significant figures as received from the bioanalytical laboratory
- $t_{max}$, $t_{last}$will be presented as received in the data, usually to 2 decimal places
- $AUC_{(0-12)}$and $t_{1/2}$ - will be presented to 3 significant figures

For PK parameter data the descriptive statistics will be presented according to the following rules:

- $C_{ss}$, $C_{max}$, $C_{1.5}$, $C_3$, $AUC_{(0-8)}$ and $t_{1/2}$- all descriptive statistics will be presented to 4 significant figures with the exception of the minimum and maximum which will be presented to 3 significant figures and n which will be presented as integers

#### 6.5.7.8 Dose Proportionality

Dose proportionality will not be formally analyzed but will be summarized descriptively using dose normalized PK parameters $C_{max}$ and $AUC_{(0-8)}$.

#### 6.5.7.9 (Relationship between exposure parameters and virologic endpoints

The response-response relationship between Plasma PK parameters ($AUC_{0-8,}$ $C_{max}$ and trough concentration, pre-dose at day 3) and efficacy endpoint of change from baseline in SARS-CoV-2 RNA at day 5 will be analyzed using a simple linear model. The paired concentration and efficacy endpoint(s) will be plotted with a fitted regression line superimposed. Additional statistical models will be explored if data warrant.

## 6.6 Safety

### 6.6.1 Extent of Exposure

Exposure will be defined in terms of numbers of doses taken. The percentage of expected exposure received will be calculated as the number of doses taken/10 expected doses and will be presented descriptively by study drug.

Where timing of dose is unavailable for a day but dosing is recorded the participant will be imputed to have received both doses of study drug.

### 6.6.2 Adverse Events

All adverse events (AEs) recorded on the eCRF will be coded using the MedDRA dictionary Version 23.1 (or a later version if updated during the study)].

All AE data will be listed by study group. Furthermore, all EIDD-2801 study groups will be pooled and presented as All EIDD-2801. In addition, corresponding listings of SAEs, AEs leading to discontinuation of study drug and AEs resulting in death will be produced.

The number and percentage of participants reporting each AE will be summarized for each study group and overall, by System Organ Class (SOC) (sorted alphabetically) and Preferred Term (PT) (sorted by descending overall total) for the Safety population.

The relationship between an AE and study drug is assessed as related or not related. A study drug-related AE is an AE considered by the investigator as related to study drug or with unknown/missing relationship to study drug.

An overview table will summarize the number and percentage of participants with at least one of the following AEs, where participants with more than one AE in a particular category are counted only once in that category:

- any AE;
- any AE by maximum grading (mild, moderate, severe, potentially life-threatening, death);
- study drug-related AE;
- SAE;
- AE leading to study drug discontinuation;
- Study drug-related SAE;
- SAE leading to death;
- Any grade 3/4 AE
- Any deaths

The overview table will also summarize the number of the following AEs:

- any AE;
- any AE by maximum grading (mild, moderate, severe, potentially life-threatening, death);
- study drug-related AE;
- SAE;
- AE leading to study drug discontinuation;
- Study drug-related SAE;
- SAE leading to death;
- Any grade 3/4 AE
- Any deaths

The number and percentage of participants reporting each AE will be summarized by System Organ Class (SOC) and Preferred Term (PT) for the Safety population. Tables will be sorted alphabetically by SOC. PTs will be sorted by descending overall total. The following summaries will be produced:

- AEs, by SOC and PT;
- AEs by PT;
- AEs related to study drug, by SOC and PT;
- AEs by maximum grade, by SOC and PT;
- AEs leading to study drug discontinuation, by SOC and PT;
- AEs related to study drug causing discontinuation from study drug, by SOC and PT;
- SAEs, by SOC and PT;
- SAEs related to study drug, by SOC and PT;
- Grade 3 or 4 AEs, by SOC and PT;
- AEs leading to death, by SOC and PT

In the above summaries, participants with more than one AE within a particular SOC are counted only once for that SOC. Similarly, participants with more than one AE within a particular PT are counted only once for that PT. For summaries by maximum grade, participants with multiple AEs within a particular SOC or PT will be counted under the category of their most severe AE within that SOC or PT. AEs with missing intensity/severity will be included (as severe) in the overall count of participants with AEs, but will not be included in the counts of participants with AEs within a SOC or PT.

The following listings will be produced:

- All deaths
- All SAEs

- All AEs leading to discontinuation of study drug

No statistical comparisons of AEs between study groups will be performed.

### 6.6.3 Laboratory Evaluations

Data for the following hematology, blood chemistry, and urinalysis analytes recorded in the eCRF will be listed and summarized by study group and visit. If data for any additional analytes are also recorded, then these will be listed only.

| Complete Blood Counts (CBC) | Comprehensive Metabolic Panels (CMP) | Urinalysis |
|---|---|---|
| Red Blood Cell Count<br>Hematocrit<br>Hemoglobin<br>White Blood Cell Count<br>Eosinophils<br>Basophils<br>Lymphocytes<br>Neutrophils<br>Monocytes<br>Immature granulocytes<br>Platelets | Alanine aminotransferase (ALT)<br>Aspartate aminotransferase (AST)<br>Total Bilirubin<br>Alkaline phosphatase<br>Albumin<br>Total protein<br>Glucose<br>Calcium<br>Creatinine<br>Estimated GFR<br>Blood Urea Nitrogen<br>Potassium<br>Sodium<br>Chloride<br>Carbon Dioxide<br>Anion Gap<br>BUN/Creatinine ratio<br>AST/ALT ratio<br>Amylase<br>Lipase | Red blood Cell Count<br>Glucose<br>White Blood Cell Count<br>Proteins<br>Nitrites<br>pH<br>Ketones<br>Bilirubin<br>Blood<br>Leukocyte<br>Urobilinogen<br>Hyaline casts<br>Granular casts<br>Epithelial cells<br>Bacteria<br>Crystals |

All laboratory data will be reported in International System of Units (SI)/Conventional units. Out-of-reference-range values will be flagged as high (H) or low (L) in the listings.

For analysis purposes, values preceded by a "<" or a ">"sign (i.e. those below or above the limits of quantification) will be considered equal to the lower or upper limit of quantification, respectively.

Laboratory data will be summarized by visit using standard descriptive statistics for the Safety population. Changes from baseline will also be summarized.

The number and percentage of participants with treatment emergent laboratory toxicities (an increase of at least one grade from baseline, or any toxicity where baseline grade is 0) with a lab toxicity grade of 3 or 4 will be tabulated by study group.

The following changes in laboratory parameters will be dichotomized and the number and percentage of participants who achieve each threshold will be tabulated by study group and visit:

- A decrease in hemoglobin from baseline by >1 g/dL or to <9 g/dL
- A decrease in platelet count from baseline by >50,000/µL or to <75,000/µL
- Aspartate aminotransferase (AST) ≥ 3x the upper limit of normal
- Alanine aminotransferase (ALT) ≥ 3x the upper limit of normal
- Amylase ≥ 3x the upper limit of normal
- Lipase ≥ 3x the upper limit of normal

For each laboratory analyte, the baseline value will be defined as last scheduled value collected prior to the first dose of study drug. Assessments carried out on the day of first study drug administration are considered to have taken place before the study drug administration, if the corresponding times have not been recorded. For post-baseline, only data from scheduled visits will be included in the summary tables. All measurements will be included in listings and will be presented including the toxicity grade.

### 6.6.4 Vital Signs

The following vital signs will be listed and summarized by study group and visit.

- systolic and diastolic blood pressure (mmHg);
- heart rate (bpm);
- respiration rate (breaths/min);
- body temperature (°C)
- mean arterial pressure (mmHg)
- oxygen saturation, $SpO_2$ (%)

Vital signs data and changes from baseline in vital signs will be summarized by visit using standard descriptive statistics for the Safety population. The baseline value will be defined as last scheduled value collected prior to the first dose of study drug. Assessments carried out on day of first study drug administration are considered to have taken place before the study drug administration, if the corresponding times have not been recorded. For post-baseline, only data from scheduled visits will be included in the summary tables. If multiple vital sign measurements are available for a participant for the same visit the average will be calculated and used in the summary tables.

### 6.6.5 Electrocardiograms

An overall Investigator assessment of ECGs will be collected during the study (categories "normal", "abnormal, not clinically significant" and "abnormal, clinically significant"). ECG assessments will be presented in listings.

### 6.6.6 Physical Examination

Abnormalities identified from physical examinations are recorded in the eCRF as Medical History or Adverse Events as appropriate and will be listed and summarized as such [See Sections 6.4.1 (Medical History) and 6.6.2 (Adverse Events)].

### 6.6.7 Other Safety Variables – Not Applicable

## 6.7 Interim Analysis

Interim analyses are planned after 25% (n=15) and 50% (n=30) of planned participants reach day 14 after the initiation of study drug. Blinded data will be reviewed by the principal investigators and the sponsor. No formal interim analysis of the planned virological efficacy or clinical endpoints are planned so no adjustment is required to control for the type I error. Data to be reviewed will include blinded summaries of the primary efficacy endpoint (achievement of undetectable viral RNA by day 5 in NP swabs) and the primary safety endpoints. The interim analyses will be used to inform sponsor decisions about whether to continue, amend, or stop the study.

A safety review committee (SRC), composed of the principal investigator for each study site and the medical monitor, will be established. The Committee will review blinded safety data at regular intervals. SRC will determine if the study enrollment or study dosing should be interrupted or if study enrollment and study dosing may continue according to the protocol. Full details of the composition, responsibilities and procedures of the SRC are described in the SRC Charter.

# 7. Changes in Planned Analysis

The protocol v5.0 specifies that the time to clearance of viral RNA in NP swabs by qPCR should be analyzed as a secondary virologic endpoint. This SAP presents the number and proportion with detectable virus at each timepoint but does not formally estimate time to clearance of viral RNA in NP swabs.

The protocol v5.0 specifies that the number of acquired single-nucleotide polymorphisms in SARS-CoV-2 genomes by days 5 and 11 in NP swabs by viral sequencing should be analyzed. The analysis plan for this endpoint will be described elsewhere and will not be included in this SAP or the associated TFL shells.

The protocol v5.0 states that the cumulative incidence, risk difference and 95% CI will be calculated for the primary safety endpoints for each study arm at interim analyses. The assessment of safety specified for these endpoints will be as described in section 6.6.2.

# 8. Data Issues

This section is not required at this time, but will be populated in a future approved version of this document.

# 9. References

1 ICH. *Statistical Principles for Clinical Trials*, Guideline E9, 1998. Available at http://www.emea.eu.int/pdfs/human/ich/036396en.pdf

2 CPMP. *Points to Consider on Missing Data*. EMEA: London, 2001. Available at http://www.emea.eu.int/pdfs/human/ewp/177699EN.pdf

3 Phillips A and Haudiquet V. *ICH E9 guideline "Statistical principles for clinical trials": a case study*. Statistics in Medicine 2003; 22:1-11

4 Brown D J. *ICH E9 guideline "Statistical principles for clinical trials": a case study. Response to A. Phillips and V. Haudiquet.* Statistics in Medicine 2003; 22:13-17

5 ICH. *ICH E3 Guideline: Structure and Content of Clinical Study Reports Questions & Answers*, 2012. Available at http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E3/E3_QAs_R1_Step4.pdf

6 Wölfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Müller MA, Niemeyer D, Jones TC, Vollmar P, Rothe C, Hoelscher M, Bleicker T, Brünink S, Schneider J, Ehmann R, Zwirglmaier K, Drosten C, Wendtner C. *Virological Assessment of Hospitalized Patients With COVID-2019*. Nature. 2020 Apr 1. doi: 10.1038/s41586-020-2196-x. 32235945

# 10. Appendices

## Appendix 1: Document History

| Document Version, Status, Date | Summary/Reason for Changes |
|---|---|
| Version 2.0, Final, 22-Dec-2020 | Final version of 1.4 update |
| Version 1.4, Draft, 22-Dec-2020 | Minor amendment for Ridgeback comments |
| Version 1.3, Draft, 21-Dec-2020 | Incorporating review comments from Ridgeback |
| Version 1.2, Draft, 09-Dec-2020 | Changes to reflect protocol v5.0 update |
| Version 1.1, Draft, 09-Oct-2020 | Changes to reflect protocol v4.0 update |
| Version 1, Final, 03-Sep-2020 | Not applicable; the first version |

## Appendix 2: Table of Contents for SAP Shells - Tables

| TFL Number | Title | Analysis Population | SRC |
|---|---|---|---|
| 14.1.1.1 | Participant Disposition | Screened | Y |
| 14.1.1.2 | Participant Disposition (Study Part) | Screened | Y |
| 14.1.2 | Participant Enrollment by Site | Randomized | N |
| 14.1.3.1 | All Protocol Deviations | ITT | Y |
| 14.1.3.2 | Important Protocol Deviations | ITT | N |
| 14.1.4.1 | Demographic and Important Baseline Characteristics | Safety | Y |
| 14.1.4.2 | Demographic and Important Baseline Characteristics | ITT | N |
| 14.1.4.3 | Demographic and Important Baseline Characteristics (Study Part) | Safety | N |
| 14.1.4.4 | Demographic and Important Baseline Characteristics (Study Part) | ITT | N |
| 14.1.5 | Medical History | Safety | N |
| 14.1.6.1 | Prior Medications | Safety | N |
| 14.1.6.2 | Concomitant Medications | Safety | N |
| 14.2.1.1 | Undetectable SARS-CoV-2 RNA by Day 5 by qPCR in NP Swabs | ITT | N |

| | | | |
|---|---|---|---|
| 14.2.1.2 | Undetectable SARS-CoV-2 RNA by Day 5 by qPCR in NP Swabs by Use of Remdesivir | ITT | N |
| 14.2.1.3 | Undetectable SARS-CoV-2 RNA by Day 5 by qPCR in NP Swabs by COVID-19 Risk Group | ITT | N |
| 14.2.1.4 | Change in SARS-CoV-2 RNA by qPCR in NP Swabs | EAS | N |
| 14.2.1.5 | Change in SARS-CoV-2 RNA by qPCR in NP Swabs by Use of Remdesivir | EAS | N |
| 14.2.1.6 | Change in SARS-CoV-2 RNA by qPCR in NP Swabs by COVID-19 Risk Group | EAS | N |
| 14.2.1.7 | Longitudinal Analysis of SARS-CoV-2 RNA by qPCR in NP Swabs | EAS | N |
| 14.2.1.8 | Longitudinal Analysis of SARS-CoV-2 RNA by qPCR in NP Swabs by Use of Remdesivir | EAS | N |
| 14.2.1.9 | Longitudinal Analysis of SARS-CoV-2 RNA by qPCR in NP Swabs by COVID-19 Risk Group | EAS | N |
| 14.2.1.10 | Change from Baseline in SARS-CoV-2 RNA by qPCR in NP swabs | EAS | N |
| 14.2.1.11 | Change from baseline in SARS-CoV-2 RNA by qPCR in NP swabs by Use of Remdesivir | EAS | N |
| 14.2.1.12 | Change from baseline in SARS-CoV-2 RNA by qPCR in NP swabs by COVID-19 Risk Group | EAS | N |
| 14.2.1.13 | Individual Rate of SARS-CoV-2 RNA Decline | EAS | N |
| 14.2.1.14 | Individual Rate of SARS-CoV-2 RNA Decline by Use of Remdesivir | EAS | N |
| 14.2.1.15 | Individual Rate of SARS-CoV-2 RNA Decline by COVID-19 Risk Group | EAS | N |
| 14.2.1.16 | Summary of Risk Factors for Severe COVID-19 | Safety | N |
| 14.2.2.1 | Undetectable Viral Titers by Infectivity Assay in NP Swabs | EAS | N |
| 14.2.2.2 | Undetectable Viral RNA by Infectivity Assay in NP Swabs in | EAS | N |

| | | | |
|---|---|---|---|
| | Patients With Positive Infectious RNA at Baseline | | |
| 14.2.3.1 | Summary of Peak WHO Ordinal Scale for Clinical Improvement | Safety | N |
| 14.2.3.2 | Summary of Requirement for Additional Antivirals | Safety | N |
| 14.2.3.3 | Summary of Requirement for Supplemental Oxygen During the First 28 Days | Safety | N |
| 14.2.3.4 | Summary of Requirement for Mechanical Ventilation | Safety | N |
| 14.2.3.5 | Summary of Requirement for Intensive Care Unit | Safety | N |
| 14.2.4.1 | Summary of Requirement for Hospitalization | Safety | N |
| 14.2.4.2 | Time Until On Room Air Without Requirement For Supplemental Oxygen | Safety | N |
| 14.2.4.3 | Time to Resolution of COVID-19 Symptoms | Safety | N |
| 14.2.4.4 | Summary of 2-point Decrease in WHO Ordinal Scale for Clinical Improvement | Safety | N |
| 14.2.4.5 | Change from Baseline in Cytokine/Inflammatory Biomarkers | Safety | N |
| 14.2.5.1 | Summary of Plasma Concentrations of EIDD-2801 (ng/mL) | PK | N |
| 14.2.5.2 | Summary of Plasma Concentrations of EIDD-1931 (ng/mL) | PK | N |
| 14.2.5.3 | Summary of Pharmacokinetic Parameters of EIDD-1931 | PK | N |
| 14.3.1.1 | Summary of Study Drug Exposure | Safety | Y |
| 14.3.2.1 | Summary of Adverse Events by Treatment Group | Safety | Y |
| 14.3.2.2 | Summary of Adverse Events by Treatment Group and Use of Remdesivir | Safety | N |
| 14.3.2.3 | Summary of Adverse Events by Treatment Group and COVID-19 Risk Group | Safety | N |

| | | | |
|---|---|---|---|
| 14.3.2.4 | Adverse Events by System Organ Class and Preferred Term | Safety | Y |
| 14.3.2.5 | Adverse Events by System Organ Class and Preferred Term and Use of Remdesivir | Safety | N |
| 14.3.2.6 | Adverse Events by System Organ Class and Preferred Term and COVID-19 Risk Group | Safety | N |
| 14.3.2.7 | Adverse Events by Preferred Term | Safety | N |
| 14.3.2.8 | Adverse Events by Preferred Term and Use of Remdesivir | Safety | N |
| 14.3.2.9 | Adverse Events by Preferred Term and COVID-19 Risk Group | Safety | N |
| 14.3.2.10 | Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug | Safety | Y |
| 14.3.2.11 | Adverse Events by System Organ Class, Preferred Term and Maximum DAIDS Grade | Safety | Y |
| 14.3.2.12 | Adverse events Leading to Discontinuation of Study Drug by System Organ Class and Preferred Term | Safety | Y |
| 14.3.2.13 | Serious Adverse Events by System Organ Class and Preferred Term | Safety | Y |
| 14.3.2.14 | Serious Adverse Events Related to Study Drug Treatment by System Organ Class and Preferred Term | Safety | Y |
| 14.3.2.15 | Grade 3 or 4 Adverse Events by System Organ Class and Preferred Term | Safety | Y |
| 14.3.2.16 | Grade 3 or 4 Adverse Events by System Organ Class and Preferred Term and Use of Remdesivir | Safety | N |
| 14.3.2.17 | Grade 3 or 4 Adverse Events by System Organ Class and Preferred Term and COVID-19 Risk Group | Safety | N |
| 14.3.3.1 | Number of Participants with Adverse Events with Outcome of Death by System Organ Class and Preferred Term | Safety | Y |

| | | | |
|---|---|---|---|
| 14.3.3.2 | Listing of Deaths | Safety | Y |
| 14.3.3.3 | Listing of SAEs | Safety | Y |
| 14.3.3.4 | Listing of AEs Leading To Discontinuation of Study Treatment | Safety | Y |
| 14.3.4.1.1 | Complete Blood Count and Comprehensive Metabolic Panel Laboratory Variables Over Time | Safety | Y |
| 14.3.4.1.2 | Treatment Emergent Chemistry Laboratory Abnormalities | Safety | N |
| 14.3.4.1.3 | Complete Blood Count and Comprehensive Metabolic Panel Laboratory Variables Changes Greater than Pre-specified Thresholds Over Time | Safety | Y |
| 14.3.4.1.4 | Complete Blood Count and Comprehensive Metabolic Panel Laboratory Variables Changes Greater than Pre-specified Thresholds Over Time by Use of Remdesivir | Safety | N |
| 14.3.4.1.5 | Complete Blood Count and Comprehensive Metabolic Panel Laboratory Variables Changes Greater than Pre-specified Thresholds Over Time by COVID-19 Risk Group | Safety | N |
| 14.3.4.1.6 | Grade 3 or 4 Treatment-emergent Laboratory Toxicities | Safety | Y |
| 14.3.4.1.7 | Grade 3 or 4 Treatment-emergent Laboratory Toxicities by Use of Remdesivir | Safety | N |
| 14.3.4.1.8 | Grade 3 or 4 Treatment-emergent Laboratory Toxicities by COVID-19 Risk Group | Safety | N |
| 14.3.4.2.1 | Urinalysis Laboratory Variables Over Time | Safety | Y |
| 14.3.4.2.2 | Treatment Emergent Urinalysis Laboratory Abnormalities | Safety | Y |
| 14.3.4.2.3 | Treatment Emergent Urinalysis Laboratory Abnormalities by Use of Remdesivir | Safety | N |
| 14.3.4.2.4 | Treatment Emergent Urinalysis Laboratory Abnormalities by COVID-19 Risk Group | Safety | N |
| 14.3.4.3.1 | Summary of Vital Signs by Study Visit | Safety | Y |

| | | | |
|---|---|---|---|
| 14.3.4.3.2 | Summary of Vital Signs by Study Visit by Use of Remdesivir | Safety | N |
| 14.3.4.3.3 | Summary of Vital Signs by Study Visit by COVID-19 Risk Group | Safety | N |
| 14.3.4.4.1 | Summary of Electrocardiogram Findings by Study Visit | Safety | Y |
| 14.3.4.4.2 | Summary of Electrocardiogram Findings by Study Visit by Use of Remdesivir | Safety | N |
| 14.3.4.4.2 | Summary of Electrocardiogram Findings by Study Visit by COVID-19 Risk Group | Safety | N |

## Appendix 3: Table of Contents for SAP Shells - Figures

| TFL Number | Title | Analysis Population | SRC |
|---|---|---|---|
| 14.2.5.4 | Arithmetic Mean Pharmacokinetic Concentration-time Profiles – EIDD-2801 | PK | N |

## Appendix 4: Table of Contents for SAP Shells - Listings

| TFL Number | Title | Analysis Population | SRC |
|---|---|---|---|
| 16.2.1 | ParticipantDisposition | Screened | Y |
| 16.2.2 | Participants with Protocol Deviations | Safety | Y |
| 16.2.3 | Demographic and Baseline Characteristics | Safety | N |
| 16.2.4 | Medical History | Safety | N |
| 16.2.5 | Prior and Concomitant Medication | Safety | N |
| 16.2.6 | Administration of Study Drug | Safety | N |
| 16.2.7 | ParticipantWithdrawal | Safety | Y |
| 16.2.8 | Virologic Sampling and Results | Safety | N |
| 16.2.9 | Individual Pharmacokinetic Parameters | Safety | N |
| 16.2.10 | Individual Pharmacokinetic Concentration Data | Safety | N |
| 16.2.11 | Hospitalization | Safety | N |
| 16.2.12 | Chest Radiography | Safety | N |

| | | | |
|---|---|---|---|
| 16.2.13 | Adverse Events | Safety | Y |
| 16.2.14 | Clinical Laboratory Data: Complete Blood Count | Safety | Y |
| 16.2.15 | Clinical Laboratory Data: Comprehensive Metabolic Panel | Safety | Y |
| 16.2.16 | Clinical Laboratory Data: Urinalysis | Safety | Y |
| 16.2.17 | Pregnancy Tests | Safety | N |
| 16.2.18 | Vital Signs | Safety | N |
| 16.2.19 | Electrocardiograms | Safety | N |
| 16.2.20 | Physical Examination | Safety | N |
| 16.2.21 | Serology Testing | Safety | N |
| 16.2.22 | WHO Ordinal Scale for Clinical Improvement | Safety | N |