Statistical Analysis Plan

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1 Abbreviations and Definitions

Abbreviation or Specialist Term	Explanation
ACE-2	angiotensin-converting enzyme 2
AE	Adverse event
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC_{0-8}	Area under the curve from time zero to 8 hours
AUC_{inf}	Area under the curve from time zero to infinity
BioAegis	BioAegis Therapeutics, Inc. Or Sponsor
BiPAP	Bilevel positive airway pressure
BUN	Blood urea nitrogen
CAP	Community-acquired pneumonia
CBC	Complete blood count
C_{max}	Maximum concentration
CMH	Cochran-mantel-Haenszel
COPD	Chronic obstructive pulmonary disease
COVID-19	Coronavirus 2019
CPAP	Continuous positive airway pressure
CPK	Creatine phosphokinase
CRO	Contract research organization
CRP	C-reactive protein
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CURB-65	Confusion, Urea >7 mmol/L, Respiratory rate ≥30/min, Blood pressure systolic <90 or diastolic ≤60, and age ≥65 years
CXR	Chest x-ray
CYP450	Cytochrome P450
DBL	Database Lock
DSMB	Data and Safety Monitoring Board
ECMO	Extracorporeal membrane oxygenation
eCRF	Electronic case report form
EDC	Electronic data capture
EKG	Electrocardiogram
EOS	End of study
HIV	Human immunodeficiency virus
ICF	Informed consent form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
ICU	Intensive care unit
IEC	Independent ethics committee
INR	International normalized ratio
IRR	Injection-related reaction
IUD	Intrauterine device

IV	Intravenous
LDH	Lactate dehydrogenase
LLOQ	Lower Limit of Quantification
MV	Mechanical ventilation
NCI	National cancer institute
PE	Physical examination
pGSN	Plasma gelsolin
PK	Pharmacokinetics
POC	Proof of concept
PT	Preferred Term
rhu-pGSN	Recombinant human plasma gelsolin
RRT	Renal replacement therapy
RT-PCR	Reverse transcription polymerase chain reaction
SAE	Serious adverse event
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SOC	Standard of care
SOC	System Organ Class
SUSAR	Suspected unexpected serious adverse reaction
$T_{1/2}$	Terminal half-life
TEAE	Treatment-emergent adverse event
T_{max}	Time to maximum concentration
VP	Vasopressor
WHO	World health organization

2 Introduction

A Phase 2 Randomized, Double-Blind, Placebo-Controlled, Proof-of-Concept Trial to Evaluate the Efficacy and Safety of Recombinant Human Plasma Gelsolin (rhu-pGSN) Added to Standard of Care for Treatment of Subjects with Severe COVID-19 Pneumonia.

Potential subjects hospitalized with laboratory-confirmed (reverse transcription polymerase chain reaction [RT-PCR+]) or highly suspected (compatible with at least bilobar lung involvement without another plausible diagnosis) COVID-19 pneumonia will be screened within 24 hours of reaching a WHO severity score of 4 to 6, whether the severity score is attained on admission or during hospitalization.

2.1 Background

Pneumonia is an inflammatory condition of the lung primarily affecting the alveoli. It is usually caused by infection with viruses or bacteria and less commonly other microorganisms. Certain drugs and other conditions such as autoimmune diseases may cause a similar clinical picture.

Typical symptoms include a cough, chest pain, fever, and difficulty breathing. Diagnostic tools include chest x-rays (CXRs), serology, microscopy of a sputum smear and culture of the sputum. Treatment depends on the underlying cause. Pneumonia documented or presumed to be viral, bacterial, or fungal is treated with appropriate agents when available. If the pneumonia is severe, the affected person is admitted to hospital.

Pneumonia is classified according to the etiologic organism and where the infection was acquired (community or hospital facility).

Community-acquired pneumonia (CAP) is the most common type of pneumonia, and may be caused by pyogenic bacteria, atypical bacteria, viruses or fungi which often cannot be identified in real time. CAP may also have non-infectious etiologies, including allergic, immune-mediated, toxins, or drugs. CAP occurs throughout the world and is a leading cause of illness and death.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) binds to the angiotensin-converting enzyme 2 (ACE-2) receptors located to certain epithelial and endothelial cell surfaces. Lung tissue is the major, but not sole target of this novel coronavirus. The agent can cause fatal infections by eliciting an over-exuberant immune response leading to injurious lung inflammation +/- a cytokine storm. Patients may die from acute lung injury/acute respiratory distress syndrome or survive with debilitating pulmonary fibrosis. Interventions have been proposed as treatment modalities to decrease the viral load and/or to modulate the intense host reaction. Blunting of an overzealous inflammatory response can potentially improve respiratory outcomes independent of any direct antiviral effect. A coagulopathy that may result in large part from endothelial cell disruption can contribute to the pathogenesis by predisposing to disseminated microthrombi and large vessel thromboemboli. Older, hypertensive, and diabetic patients are at highest risk for complications and serious outcomes.

Plasma gelsolin (pGSN), an abundant, naturally occurring, circulating protein depleted in severe inflammatory conditions, offers similar promise in aborting lung injury, and offers a possible novel therapeutic agent in this time of crisis. Since recombinant human pGSN (rhu-pGSN) is a pathogen-indifferent treatment acting primarily on host inflammatory responses, the microbial etiology of life-threatening pneumonia is not particularly relevant.

2.2 Rationale

2.2.1 Rationale for Study

The damage inflicted by COVID-19 is primarily mediated through an overly exuberant host response to the virus, not directly by the virus itself. This overblown reaction consists of excessive and prolonged inflammation culminating in a cytokine storm and disseminated coagulopathy injuring the lungs and blood vessels. Interrupting or tempering this maladaptive process lessens further organ injury, restoring immune equilibrium and allowing tissue repair.

Plasma gelsolin plays a central regulatory role ("master switch") in diverse inflammatory pathways. A dual-pronged attack on COVID-19 concurrently reducing the inciting virus (with remdesivir or other antiviral agents) and quelling the inflammatory tsunami (with a non-toxic but powerful anti-inflammatory drug) could theoretically synergize in shutting down the COVID-19 attack better than either modality alone. The action of pGSN on multiple pathways effectively blocks unbridled immune activation without inducing undesired side-effects or dangerous immunosuppression.

2.2.2 Rationale for Starting Dose

The dosage for this trial was extrapolated from efficacious doses in animal studies of severe pneumonia. A Phase 1b/2a dose escalation study showed no drug-related or SAEs in patients with CAP administered 3 daily doses of rhu-pGSN at 6, 12, and 24 mg/kg of actual body weight.

3 Study Objectives

3.1 Primary Objective

- *To assess the efficacy (survival without organ failure on Day 14) of IV rhu-pGSN plus SOC vs placebo plus SOC (hereafter referred to as rhu-pGSN vs placebo) administered to hospitalized subjects with a primary diagnosis of COVID-19 pneumonia and a severity score of 4, 5, or 6 on the World Health Organization (WHO) 9-point severity scale.*
- *To evaluate the safety (incidence of SAEs) of IV rhu-pGSN administered to hospitalized subjects with a primary diagnosis of COVID-19 pneumonia and a severity score of 4, 5, or 6 on the WHO 9-point severity scale.*

3.2 Secondary Objectives

- *To further assess the efficacy of IV administered rhu-pGSN*
- *To measure changes in the WHO 9-point severity scale for SOC ± rhu-pGSN*
- *To evaluate the effect of administered rhu-pGSN on survival rates*
- *To assess the relationship of pGSN levels (and other biomarkers) at baseline with clinical outcomes*
- *[OPTIONAL] To follow the PK of administered rhu-pGSN*

3.3 Immunogenicity Objective

- *To investigate the development of antibodies against pGSN post-treatment in rhu-pGSN vs placebo recipients compared to baseline.*

4 Study Design

4.1 Overview

This is a randomized, double-blind, placebo-controlled, multicenter Phase 2 study to evaluate the efficacy and safety of rhu-pGSN plus SOC in subjects with severe COVID-19 pneumonia. Potential subjects hospitalized with laboratory-confirmed (reverse transcription polymerase chain reaction [RT-PCR+]) or highly suspected (compatible with at least bilobar lung involvement without another plausible diagnosis) COVID-19 pneumonia will be screened within 24 hours of reaching a WHO severity score of 4 to 6, whether the severity score is attained on admission or during hospitalization.

4.2 Sample Size Justification

The primary endpoint is difference between treatments in the proportion of surviving subjects off vasopressors, the ventilator, and dialysis on Day 14. Here the power for the study is computed for the expected increase in proportion of surviving subjects without these supports at Day 14 after start of study treatment. A total sample size of N=54 has ~80% power to yield a statistically significant (alpha=0.2 1-sided) difference if the TRUE underlying proportions are 20% and 5% for placebo plus SOC and rhu-pGSN plus SOC, respectively. The minimum OBSERVED difference from placebo plus SOC proportion 20% that yields statistical significance is 8.4% (20% vs 11.6%). As this is a pilot Phase 2 POC trial in an infection with no approved therapy and false negative error (100% minus power) is equally as important as false positive error, the one-sided type 1 error is set at 0.2. Thus, the trial is adequately powered for its primary POC objective.

4.3 Randomization and Blinding

Following screening, subjects qualified for study entry will be randomized to receive rhu-pGSN or placebo during the treatment period. Randomization will be done centrally using manual methods. All eligible subjects will be assigned a randomization number.

The investigational site team and the subject will be kept blinded to the treatment allocation of each participant. Only the designated pharmacist(s) will be unblinded to the treatment allocation. A manual system to randomly assign a treatment allocation. The treatment allocation will be available to the unblinded pharmacist(s).

Details regarding Randomization and Blinding is maintained in the following study documents:

- BTI-202_Randomization Plan, version 1.00 (dated 28-Jul-2020)
- BTI-202_Unblinding Plan, version 1.00 (dated 28-Jul-2020)

4.4 Unblinding

The unblinded pharmacist(s) will prepare sterile syringes with filters consisting of 12 mg/kg rhu-pGSN or normal saline (Section 8.3) according to the treatment allocation for each subject.

There is no antidote for rhu-pGSN. Unblinding should only be performed if knowledge of the treatment assignment will change the planned management of a medical condition. If possible, prior to unblinding, the need to unblind should be discussed with the Medical Monitor or Sponsor's Chief Medical Officer; however, this should not delay unblinding if the Investigator believes it is necessary. Each case of unblinding will be documented and documentation will be stored separately by the unblinded pharmacist.

Subjects that are unblinded may be withdrawn from the study. The decision to withdraw a subject from the study because of unblinding should be discussed with the Sponsor. If the subject is withdrawn, the Investigator or designee must record the date and reason for withdrawal on the appropriate eCRF for that subject.

4.5 Inclusion/Exclusion Criteria

4.5.1 Inclusion Criteria

To be considered eligible to participate in this study, a subject must meet all the inclusion criteria listed below:

1) *Hospitalized with laboratory-confirmed (RT-PCR+) or highly suspected (compatible with at least bilobar lung involvement without another plausible diagnosis) COVID-19*
2) *Age ≥18 years*
3) *Weight ≤100 kg*
4) *Within 24 hours of reaching a WHO severity score of 4-6 either:*
    a) *At admission*
    b) *While already hospitalized.*
5) *Informed consent obtained from subject/next of kin/legal proxy*
6) *Primary admitting diagnosis of pneumonia supported by a compatible clinical presentation with a documented infiltrate consistent with pneumonia on CXR or CT, as assessed by the admitting emergency department (ED), clinic, or ward physician or equivalent caregiver*
    a) *Recommended (not mandatory) guidance/discretionary criteria defining patients with pneumonia satisfying all 4 categories below:*
        i) *At least 2 symptoms: difficulty breathing, cough, production of purulent sputum, or chest pain*
        ii) *At least 2 vital sign abnormalities: fever, tachycardia, or tachypnea (thresholds -- fever: oral or core temperature >100.4°F [38°C]; heart rate >100 beats/min; respiratory rate >24/min)*
        iii) *At least one finding of other clinical signs and laboratory abnormalities: hypoxemia (O2 saturation <90%), clinical evidence of pulmonary consolidation, or leukocytosis ≥1.5x104 or leukopenia <4x103*
        iv) *Chest imaging or CT chest showing at least bilobar pulmonary infiltrates*

(1) *Principal Investigator (PI) to note radiologic findings in the eCRF*

(2) *Radiology report to be placed in the eCRF*

(3) *A copy of the radiograph attached to be saved for review*

b) *A hyperinflammatory status (defined by increased ferritin ≥500 µg/L, D-dimer ≥1000 ng/mL, or CRP ≥75 mg/L)*

7) *During the course of the study starting at screening and for at least 6 months after their final study treatment:*

a) *Female subjects of childbearing potential must agree to use 2 medically accepted birth control methods*

b) *Male subjects with a partner who might become pregnant must agree to use reliable forms of contraception (i.e., vasectomy, abstinence), or an acceptable method of birth control must be used by the partner*

c) *All subjects must agree not to donate sperm or eggs (ovocytes)*

4.5.2 Exclusion Criteria

To be eligible for entry into the study, the subject must not meet any of the exclusion criteria listed below:

1. *Only negative RT-PCR tests for COVID-19 (in the absence of a PCR positive test) during the evaluation of the present illness*
2. *Extracorporeal membrane oxygenation (ECMO)*
3. *Pregnant or lactating women*
4. *Active underlying cancer treated with systemic chemotherapy or radiation therapy during the last 30 days*
5. *Transplantation of hematopoietic or solid organs*
6. *Chronic mechanical ventilation or dialysis*
7. *Otherwise unsuitable for study participation because of chronic, severe, end-stage, and life-limiting underlying disease unrelated to COVID-19 likely to interfere with management and assessment of acute pneumonia, only comfort or limited (non-aggressive) care is to be given, or life expectancy <6 months unrelated to acute COVID infection in the opinion of the Investigator*

Notes:

- *Participants refusing PK blood samplings can remain in the trial.*
- *Participants with superinfection in addition to COVID-19 are eligible.*
- *Caregivers can decide whether any other medications (investigational or otherwise) should be administered.*

4.6 Treatment Allocation

Subjects will be randomized in a 1:1 ratio to receive SOC plus IV rhu-pGSN or placebo during the treatment period.

5 Assessment Schedule

Visit	Screening	Baseline/ Treatment	Continued Treatment	Follow-up Visits					Early Term/ End of Study Visit
Day	-1[a]	1[a]	2	3	7 ± 1	14 ±2	28 ±2	60 ±2	90 ± 4
Informed consent	X								
Eligibility assessment	X	X							
Randomization if appropriate		X							
Medical history/signs and symptoms	X	X[b]							
WHO Severity Score	X	X	X	X	X	X	X	X	X
Sputum culture[c, d]	X								
Blood or urine pregnancy	X (for women of childbearing potential only)						X		X (for women of childbearing potential only)
HIV	Not required (can be done at the discretion of caregivers)								
Confirm COVID-19 pneumonia (CXR or CT, RT-PCR for COVID-19)[c, d, e]	X[e]					X[e]	X[e]		
CURB-65 score	X			X	X	X	X	X	
Physical exam	X	X[b]	X	X	X	X	X	X	X
Abbreviated Mental Test Score	X			X	X	X	X	X	
Vital signs, including pulse oximetry[f]	X	X	X	X	X	X	X	X	X
EKG[d, g]	X	X[b]	X	X					X
Sampling for pGSN levels (including PK)[h]		X	X	X[i]	X	X	X	X	X
CBC with differential and reticulocyte count; PT (INR)/PTT[d]	X	X[b]	X	X	X	X	X	X	X
Comprehensive metabolic profile (including amylase or lipase)[d]	X	X[b]	X	X	X	X	X	X	X
Biomarker sampling[j]		X[b]		X	X	X	X	X	
Anti-rhu-pGSN antibody sampling (immunogenicity)[k]		X[b]					X		X
Study drug administration[l]		X[l, m]	X[n]						
AEs (only SAEs after Day 14)		X	X	X	X	X	X	X	X
Con meds	X	X	X	X	X	X	X	X	X

Abbreviations: AEs=adverse events; CBC=complete blood count; Con meds=concomitant medications; CRP=C-reactive protein; CT=computed tomography; CURB-65=Confusion, Urea >7 mmol/L, Respiratory rate ≥30/min, Blood pressure systolic <90 or diastolic ≤60, and age ≥65 years (score); CXR=chest x-ray; EKG=electrocardiogram; HIV=human immunodeficiency virus; IL=interleukin; INR=international normalized ratio;

PK=pharmacokinetic; PT=prothrombin time; PTT=partial thromboplastin time; RT-PCR=reverse transcription polymerase chain reaction; SOC=standard of care; Term=termination; TNF=tumor necrosis factor; WHO=World Health Organization.

[a] Day 1 is the first day of study treatment. Baseline tests (including blood draws) should be performed prior to administration of the first dose. Screening tests may also be performed on Day 1 prior to study treatment if necessary, as long as these tests cannot affect eligibility. If Dose 1 is administered in the evening of Day 1, Dose 2 would be given on the second calendar day and Dose 3 would be given on the third calendar day.

[b] Test/assessment does not have to be repeated if performed within the prior 24 hours unless dictated by SOC.

[c] Collect sputum sample as soon as possible if not collected at the time of hospital admission. The microbiology lab is encouraged to also perform sputum Gram-stains, antigen detection, immunoassay, and RT-PCR diagnostic tests when available. If fevers or chills are present, 2 sets of blood cultures are recommended at the discretion of the caregivers.

[d] To be performed if/when indicated by SOC.

[e] At screening, document radiographic evidence (CXR, or CT scan if CXR is inadequate) of COVID-19 pneumonia if not already completed in the previous 48 hours per SOC. On Days 14 and 28, repeat RT-PCR for COVID-19 and repeat CXR, or CT scan if CXR is inadequate, are encouraged but not mandatory.

[f] Record blood pressure, oral temperature, respiration rate, and heart rate, as well as pulse oximetry. To be measured during study drug administration at the following time points: predose, at the end of administration, and 30 minutes after the end of administration.

[g] When EKGs are to be collected at the same time point as a blood collection, EKGs should be collected first. At screening, 3 serial, resting, supine 12-lead EKGs are to be conducted within 10 minutes total time. All other ECGs are single recordings.

[h] Blood for PK will be drawn for Dose #1 within 15 minutes predose, and at 1 (±15 min), 2 (±15 min), 6 (±30 min), and 12 (±30 min) hours after the end of administration (but prior to Dose #2); and for Dose #3 within 15 minutes predose, and at 1 (±15 min), 2 (±15 min), 6 (±30 min), 12 (±30 min), and 24 (±30 min) hours after the end of administration. Samples should be spun and plasma frozen and sent to a central lab for analysis.

[i] Blood for PK will be collected 24 hours after the end of study drug administration given on Day 2 so the last sample will be obtained Day 3.

[j] Collect blood for measurement of ferritin, D-dimer, CRP, and procalcitonin for evaluation at local laboratory; save an approximate 10 mL aliquot of blood plasma or serum to be frozen at -20°C for subsequent biomarker assays (likely to include, but not limited to IL1β, IL6, IL10, TNF, etc.) for analysis at the central laboratory.

[k] Sample to be sent to a central lab for analysis.

[l] Study drug to be administered at 0, 12, and 36 hours (± 60 minutes). Subjects are to be monitored for administration site reactions during study drug administration and for 1 hour after its completion.

[m] Initial dose must be administered no later than 12 hours after randomization. A second dose on Day 1 is to be administered 12 hours after the initial dose.

[n] Day 2 dose to be administered 24 hours after last dose administration on Day 1 (36 hours after Dose #1).

6 Interim Analysis

There is no formal interim analysis planned as per study protocol, however, an independent DSMB will be established to closely monitor the safety of subjects. The primary mission of the DSMB is to ensure that decisions are made that serve the best interests of patients volunteering for the study. Other details regarding the DSMB Meeting are mentioned in the DSMB Charter Document (version 2.0, 07-Aug-2020).

7 Efficacy and Safety Endpoints

7.1 Primary Endpoints

7.1.1 Safety and tolerability

- *Incidence of SAEs in rhu-pGSN vs placebo groups*

7.1.2 Efficacy

- *Proportion of subjects alive not on vasopressors, mechanical ventilator, and dialysis on Day 14.*

7.2 Secondary Endpoints

7.2.1 Safety and tolerability

- *Incidence, causality, and severity of AEs (graded according to the National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE] version 5.0) in rhu-pGSN vs placebo groups*
- *Frequencies of new or worsening clinically significant laboratory abnormalities in rhu-pGSN vs placebo groups*
- *Mortality rate irrespective of cause at Days 28 and 90*

7.2.2 Efficacy

- *Daily change in 9-point WHO severity score through at least Day 14*
- *All-cause mortality at Days 28 and 90; time to death (Kaplan-Meier survival analysis)*
- *Proportion of subjects alive on Days 7, 14, 28, 60, and 90 without:*
  - *Ongoing use of vasopressors*
  - *Ongoing intubation/mechanical ventilation*
  - *Ongoing residence in an ICU*
  - *New ongoing need for dialysis/renal replacement therapy (RRT)*
- *Proportion of subjects discharged to home or immediate prior residence by Day 28*
- *Days on the ventilator*
- *Length of stay (LOS) in hospital and in ICU (days)*
- *Re-admission to an acute-care hospital up to Day 90*

7.2.3 PK (Optional)

- *PK for rhu-pGSN including maximum concentration (Cmax), time to maximum concentration (Tmax), terminal half-life (T1/2), area under the curve from time zero to 8 hours (AUC0-8), area under the curve from time 0 to infinity (AUCinf) for Dose #1 within 15 minutes predose, and at 1 (±15 min), 2 (±15 min), 6 (±30 min), and 12 (±30 min) hours after end of administration (but prior to Dose #2); for Dose #3 within 15 minutes predose, and at 1 (±15 min), 2 (±15 min), 6 (±30 min), 12 (±30 min) and 24 (±30 min) hours after the end of administration (participants refusing these blood samplings can enter and remain in the trial).*

7.2.4 Immunogenicity

- *Presence of anti-pGSN antibodies on Days 1 (predose), 28, and 90*

7.3 Exploratory Endpoints

7.3.1 Biomarkers

- *Changes in biomarkers and radiologic imaging over time with treatment*
- *Relationship of baseline biomarkers to clinical outcomes*

8 Statistical Methods

8.1 General Conventions

All analyses will be done using SAS (version 9.4, SAS Institute Inc., Cary, NC, USA).

Efficacy and Safety endpoints will be analyzed in a descriptive manner. Continuous data will be reported using the following descriptive statistics:

1. Number of observations (n)
2. Mean and Standard deviation (SD)
3. Interquartile Range (IQR)
4. Minimum (min) and Maximum (max)
5. Median

In addition:

6. Geometric mean & Standard deviation
7. Coefficient of variation (CV%)
8. Geometric CV%

will be reported for plasma concentration data and PK parameters. Categorical data will be presented using frequency (n = number of subjects; m = number of events) and percentage (%).

Listings will be provided for all data recorded in eCRF to study subject profiles. All listings will be sorted by treatment, subject ID, and date (if applicable). Unscheduled visit data will only be listed and not included in summaries.

All p-values will be displayed to four decimal places, with p-values less than 0.0001 presented as '<0.0001' and p-values greater than 0.9999 presented as '>0.9999'. Minimum and maximum values will be reported in the units of collection with 3 decimals being maximum value; the mean will be presented with 1 decimal place more and the standard deviation 2 decimal places more than the units of collection. Percentages for categorical summaries will be represented to 1 decimal place.

8.2 Multiplicity Adjustment

Since there is only one primary efficacy hypothesis defined in the study as per the protocol (difference between treatments in the proportion of surviving patients off vasopressors, the ventilator, and dialysis on Day 14), multiplicity adjustment is not required for the primary endpoint. Hypothesis tests for secondary endpoints will be performed, and caution must be taken when interpreting these results. Adjusted p-values using Bonferroni method may be reported from post-hoc tests if deemed necessary.

8.3 Re-estimation of Sample Size

Exploratory analyses to compare the efficacy endpoint data from the rhu-pGSN group from this study to that of external control data may be carried out if appropriate. Sample size may be increased to improve the precision of the estimates of between-treatment comparisons if appropriate and if drug supplies are available.

9 Data handling Procedures

9.1 Handling Missing/Incomplete Data

Plasma concentration results missing, or below lower limit of quantification (LLOQ) will be set to 0 for pre-dose measurements. Missing PK parameters will be imputed at the LLOQ value. Plasma concentration results missing or below LLOQ for post-dose measurements will not be imputed.

Handling of missing data for efficacy analyses is defined in the respective sections below.

9.2 Partial dates

Partial dates are not expected for start and end dates of adverse events. Queries will be raised and resolved in case of partial dates in AE prior to database lock.

Partial dates may be imputed for medications and diseases to determine whether they are concomitant medications or concurrent diseases using the algorithm given below.
For medical history, end dates will be imputed as follows:

- If marked "ongoing" with no end date, then this will be considered as concurrent disease.
- If only year is present, then impute date and month as 31-DEC.
- If month and year are present, then impute date with last date of the month.
- If date and year are present, then impute month as DEC.
- If year is missing, then impute subject's last visit date in the study.

If the imputed end date is later than subject's last visit date, then the subject's last visit date will be imputed. In case of ambiguity, then the worst case is considered (that is, concurrent diseases) for safety analyses.
Example,

Partial End Date	Imputed End Date
--JUN2019	30JUN2019
-----2019	31DEC2019
12---2018	12DEC2018
14MAR----	Subject's last visit date

For concomitant medications, start dates will be imputed as follows:

- If only year is present, then impute date and month as 01-JAN.
- If month and year are present, then impute date with first date of the month.
- If date and year are present, then impute month as month as JAN.
- If year is missing, then impute subject's first IMP date in the study.

If the imputed start date is earlier than subject's first IMP date, then the subject's first IMP date will be imputed. In case of ambiguity, then the worst case is considered (that is, concomitant medications) for safety analyses.

Example,

Partial Start Date	Imputed Start Date
--JUN2019	01JUN2019
-----2019	01JAN2019
12---2018	12JAN2018
14MAR----	Subject's first IMP date

Imputed dates will be used for analyses and collected dates will be recorded in database will be displayed in listings.

9.3 Handling Outliers

Safety and Efficacy endpoints will be cleaned and reviewed periodically during the course of the study. There are no outliers expected during database lock. In exceptional cases, the handling conditions for these will be discussed during the blinded review meeting prior to DBL.

9.4 Blinded Review Meeting

- Exclusion of subjects from each of the population definitions defined in Section 10 will be reviewed and finalized.
- Protocol deviation classifications will be reviewed and finalized.
- Any repeat assessments for safety and efficacy endpoints, and its inclusion in summaries will be finalized.
- Conversion factors for laboratory parameters to SI units will be confirmed.
- Any subjects who did not take treatment as planned will be reviewed.
- Timing of replacement subjects to be reviewed after discontinuation of original subjects.
- Any self-evident corrections in spelling of free text values will be confirmed.
- Incorrect derivations in EDC derived values to be verified.
- Changes from planned analyses / extent of exploratory or additional analyses will be finalized.
- Any outlier values identified during pre-final data review will be closed.

10 Analysis Sets

The membership of the analysis sets will be reviewed and finalized during the blinded review of the data conducted prior to database lock.

10.1 Screened Analysis Set

The Screened Analysis Set includes all subjects who gave informed consent.

The Screened Analysis Set will be used for summary of subject disposition. There will not be any treatment wise analysis when using the Screened Analysis Set.

10.2 All-enrolled Analysis Set

The All-enrolled Analysis Set includes all subjects who gave informed consent and enrolled in the trial. The All-enrolled set will be used to list all screened subjects.

The all-enrolled analysis set will be used for summary of subject disposition. There will not be any treatment wise analysis when using the all-enrolled analysis set.

10.3 Randomized Analysis Set

The Randomized Analysis Set includes all subjects who passed eligibility criteria and were randomized.

The Randomized Analysis Set will be used for summaries of subject disposition, demographics, baseline characteristics and protocol deviations. Subjects will be analyzed according to the treatment group they were assigned at randomization.

Note: If a subject is randomized but did not take the study drug, then the subject will be included only in the Screened, All-Enrolled and Randomized Analysis Sets. Subjects with negative COVID RT-PCR results post randomization will still be included.

10.4 Full Analysis Set

All subjects given ≥1 dose of study drug will be included in the Full Analysis Set (FAS) according to actual drug received.

The FAS is the primary analysis set to analyze all efficacy endpoints. Subject disposition, demographic and baseline characteristics of the FAS will also be presented. Subjects will be analyzed according to the treatment group they actually received. Differences between planned and actual treatment, if any, will be discussed during the blinded review meeting.

Note: if a subject had inadvertently taken the study drug without randomization and/or had negative COVID RT-PCR results post study drug administration, the subject would still be included in the Full analysis set.

10.5 Safety Analysis Set

The Safety Analysis Set includes all subjects who received at least one dose of study drug.

The Safety Analysis Set will be used for the analysis of safety. Subjects will be analyzed as treated, regardless of the randomized treatment assigned, if this differs from that to which the subject was randomized. Any differences between planned and actual treatment, if any, will be discussed during the blinded review meeting.

Note: if a subject had inadvertently taken the study drug without randomization and/or had negative COVID RT-PCR results post study drug administration, the subject would still be included in the Safety Analysis Set.

Note: FAS and Safety Analysis Set are the same as per definition. To be in line with study protocol, FAS will be used for all efficacy analysis, Safety Analysis Set will be used for all safety analysis (Adverse events, Lab values, Vital Signs, Physical Examination, EKG etc.).

10.6 Per-Protocol Analysis Set

The Per-Protocol Analysis Set includes all subjects who completed Day 14, took all three doses, and had no Important protocol deviations that may affect the primary endpoint of the study.

The exclusion of subjects from the per-protocol analysis set will be discussed and finalized during the blinded review meeting prior to DBL. Protocol deviations that can potentially unblind treatment codes will be reviewed independently by authorized personnel and its impact on population flags will be confirmed prior to DBL.

The PPAS is also used to analyze efficacy endpoints. Demographic and baseline characteristics of the PPAS will also be presented. Subjects will be analyzed according to the treatment group they actually received.

10.7 PK Analysis Set

The PK Analysis Set will include all subjects in the FAS who have sufficient concentration data to obtain reliable estimates of the key PK parameters and have no important protocol deviations that can influence the validity of the data for the PK endpoints.

PK Analysis Set will be finalized after review of concentration data post DBL and unblinding.

11 Analysis Variables

11.1 Analysis Set Flags

Analysis Set flags will be finalized and authorized by the Study Statistician and Sponsor during blinded review meeting prior to database lock as per definitions provided in Section 10. These flags will be included in the analysis datasets.

11.2 Treatment groups

All analyses will be summarized by treatment group. The following treatment groups will be defined in the analysis datasets.

- rhu-pGSN
- Placebo

11.3 Analysis Visits

All analysis datasets with measurements taken at more than one visit/time point will have analysis visit and timepoint as defined below.

Visit as in CRF	Visit Representation in summaries
Screening	-
-	Baseline

Visit as in CRF	Visit Representation in summaries
Day 1	Day 1
Day 2	Day 2
Day 3	Day 3
Day 7	Day 7
Day 14	Day 14
Day 28	Day 28
Day 60	Day 60
End of Study / Early Termination	Early Termination
End of Study / Early Termination	End of Study

The End of Study and Early Termination visits will be presented separately. Screening Visit will be summarized only in listings except for the demographic and baseline characteristics data.

A subject is considered to have attended any visit only if at least one assessment has been taken at the visit.

11.3.1 Timepoints

Vital signs and PK Samples will be collected at various timepoints, these will be included for summaries as follows:

Endpoints	Timepoint in Analysis
Vital Signs	Dose X, Pre-Dose Dose X, End of Study Drug Administration Dose X, 30 Minutes Post-Dose
Plasma concentration	Pre-Dose 1 Hour Post-Dose X Hours Post-Dose

11.3.2 Study Period

Study Periods will be assigned as follows:

- Informed Consent Date to the day before first IMP date – 'Screening'
- Date of first IMP to Day 14 – 'Treatment Period'
- Day 15 to End of Study – 'Follow-up Period'

11.3.3 Visit Imputation

For assessments where shift summaries are required (WHO Severity Score and CURB-65 Score), records will be imputed for all subjects in Safety Analysis Set in all scheduled visits and marked as 'Missing / Not Done' if either the subjects did not attend the visit or discontinued or had missing assessment at the respective visit.

11.3.4 Repeat Assessments

If there are any repeat assessments, they will be logged as unscheduled visits and the reason for unscheduled visit will be marked as repeat assessment. In such cases, these unscheduled visits will be mapped to the visit for which repeat assessment was taken. In case of multiple repeat assessments on the same day, the latest assessment will be considered for analysis.

For WHO Severity scores, if there are more than one repeat assessments on the same day, then highest non-missing score will be considered for analysis.

11.4 Study Duration

Study Duration (days) = (Date of Last Visit –First IMP Date) + 1.

11.5 Discontinued Subjects

Discontinued subjects will have safety assessments taken at Early Withdrawal visits. These will be presented separately and will not be combined with EOS if results are available.

The reason for discontinuation from the study will be mapped in the analysis as follows:

Primary reason for early discontinuation (As in CRF)	Reason for early termination from the study
Subject withdrew consent	Subject withdrew consent
Unacceptable AE	Unacceptable AE
Pregnancy	Pregnancy
Subject is unwilling or unable to continue the study or is lost to follow up	Subject unwilling / lost to follow-up
Subject is non-compliant with study procedures/study protocol	Protocol Deviation
Investigator decides that withdrawal from the study is in the best interest of the subject	At the discretion of the Investigator
Any clinically significant change in subject's medical condition (at the discretion of the Investigator)	At the discretion of the Investigator due to change in medical condition
Treatment unblinded	Treatment Unblinded
Sponsor decision to end the study	Sponsor decision to end the study
Death	Death
Other	Other

11.6 Replacement Subjects

If one of the eligible subjects is included in the study as replacement, then the subject will be flagged as replacement subject with subject ID of the replaced subject. For example, if subject XXXY is replaced, then replacement subject XXXX will be flagged as '*Replacement for XXXY*'. These flags will be used only in listings, and not in any analyses. Summaries will include data for replacement subjects like any other subject in that treatment group.

11.6.1 Common Derivations

The following variables will be derived in analyses datasets and used in summaries as per the formula below:

- BMI (kg/m^2) = Weight in kg / (Height in cm x 0.01)^2. Height from screening, and weight from respective visit will be used.
- Age (years) = ((Date of Informed consent – Date of Birth) + 1)/365.25
- QTcF (msec) = QT (msec) / (RR (msec)/1000)$^{1/3}$
- Duration (days) = (End Date – Start Date) + 1
- Start Day (days) = (Start Date – First IMP date) + 1

These variables will be derived and verified against EDC calculated values, if available. In cases where they do not match, queries will be raised. If not reconciled until database lock, derived values will be considered correct and will be used for analysis.

11.7 Baseline

All analysis datasets having measurements taken at more than one visit/time point will have baseline flags. Baseline is defined as the latest non-missing measurement prior to IMP administration including repeat assessments and unscheduled visits. In case of multiple results at the same date/time, worst result will be considered as baseline in the following order or hierarchy: Abnormal CS, Abnormal NCS, Normal, Missing.

11.7.1 Change from Baseline

Change between Baseline and post-baseline result will be calculated as:

Change from baseline = Result at Visit X – Baseline Result

11.8 Protocol Deviations

Protocol Deviations will be classified by the Sponsor as 'Important/Major' and 'Not Important'. The deviations will be reviewed during the blinded review meeting and finalized prior to DBL.

11.9 Treatment Compliance

The following variables will be derived for treatment compliance summaries:

- Cumulative IV Planned to be administered (mL) = Planned Dose for Dose 1 (mL) + Planned Dose for Dose 2 (mL) + Planned Dose for Dose 3 (mL)
- Cumulative Actual IV administered (mL) = Total amount infused for Dose 1 (mL) + Total amount infused for Dose 2 (mL) + Total amount infused for Dose 3 (mL)
- Treatment Duration (hours) = End Date and Time of Last Dose – Start Date and Time of First Dose

- Treatment Compliance (%) = $\frac{\text{Cumulative Actual IV Administered}}{\text{Cumulative Planned IV to be Admisitered}}$ x 100.

Treatment compliance is based on volume of IV administered, and not IMP dose, hence placebo group will also have this calculation done.

11.10 Medical History and Concurrent Diseases

If a condition has end date prior to first dose of IMP or if end date is missing and the Ongoing status = No, then these will be flagged as Medical / Surgical History. If a condition has end date on or after first dose of IMP or if the Ongoing status = Yes, then these will be flagged as Concurrent Diseases.

11.11 Prior and Concomitant Medications

The following will be the definitions for classification of Prior and Concomitant Medications:

Start Date	End Date	Study Period	Prior / Concomitant
Before IMP	Before IMP	N/A	Prior Medication
Before/After IMP and before Day 14	On or Before Day 14	Treatment Period	Concomitant Medication
Before/After IMP and before Day 14	After Day 14 and On or Before EOS	Treatment Period	Concomitant Medication
After Day 14	After Day 14	Follow-up Period	Concomitant Medication

Note: Worst case scenario of the medication being concomitant to the study drug administration will be considered.

11.12 Adverse Events

A Treatment-Emergent Adverse Event (TEAE) is defined as any AE that begins/ worsens after the first IMP administration.

Related Adverse Events include Possibly, Probably and Definitely Related Adverse Events. Not Related Adverse Events include Probably and Definitely not related Adverse Events.

11.13 Laboratory Assessments

Laboratory results with modifiers will be analyzed with the maximum or minimum value defined without the modifiers. For example, a value of "<5" will be considered as "5" for summaries.

11.14 EKG Measurements

Average of triplicate measurements will be calculated for the following EKG parameters at Screening: Heart rate (bpm), RR (msec), PR (msec), QRS (msec), QT (msec), QTcF (msec).

Average of triplicate measurements = (Measurement 1 + Measurement 2 + Measurement 3) / 3

Note that, if any one measurement is missing, the average of the other 2 measurements will be taken.

11.15 Unit Conversion

For laboratory parameters, units will be converted and summarized in SI units. Reference used for conversion factors will be documented in the respective footnotes.

11.16 Efficacy Endpoints

11.16.1 Hospitalization due to COVID-19

- Days in X = (End Date of X - Start Date of X) + 1
- Cumulative X Days = Sum of all (Days in X)

Note: X denotes Hospitalization, Intensive Care Unit (ICU) and Intubation / Mechanical Ventilations.

- Duration of COVID-19 illness before hospitalization (days) = (Initial Hospitalization Date – COVID-19 confirmation date) + 1

Note: The earliest COVID-19 confirmation date will be considered irrespective of whether or not it is prior to informed consent date.

If a subject has discontinued from the study and X is ongoing or the end date is missing, then X will be considered as ongoing at Day 14 for that subject. For cumulative X days calculation, disposition date will be considered as end date. If a subject had Ongoing Hospitalization at end of study, then end date is considered as subject's disposition date.
Note: X denotes Hospitalization, Intensive Care Unit (ICU) and Intubation / Mechanical Ventilations.

11.16.2 URB-65 Score

The score is an acronym for each of the risk factors measured. Each risk factor scores one point, for a maximum score of 5:

- *Confusion of new onset (defined by the Abbreviated Mental Test Score [see Appendix B] of 8 or less [2 or more incorrect answers])*
- *Blood Urea nitrogen greater than 7 mmol/l (19 mg/dL)*
- *Respiratory rate of 30 breaths per minute or greater*
- *Blood pressure less than 90 mmHg systolic or diastolic blood pressure 60 mmHg or less*
- *Age 65 or older*

11.16.3 bbreviated Mental Health Score

The questions are put to the patient. Each question correctly answered scores one point. A score of 8 or less suggests cognitive impairment at the time of testing, although further and more formal tests are necessary to confirm a diagnosis of dementia, delirium or other causes of cognitive impairment.

- *What is your age? (1 point)*
- *What is the time to the nearest hour? (1 point)*
- *Give the patient an address and ask him or her to repeat it at the end of the test. (1 point)*

- *e.g. 42 West Street*
- *What is the year? (1 point)*
- *What is the name of the office or doctor you are seeing today? (1 point)*
- *Can the patient recognize two persons (the doctor, nurse, home help, etc.)? (1 point)*
- *What is your date of birth? (day and month sufficient) (1 point)*
- *In what year was the 9-11 terrorist attack? (1 point) (other dates can be used, with a preference for dates sometime in the past)*
- *Name the present president of the USA. (1 point)*
- *Count backwards from 10 down to 1. (1 point)*

11.16.4 WHO Severity Scores

The 9-point WHO classification scheme from 0 to 8 for COVID-19 pneumonia will be applied to grade the severity of illness as follows:

- *8 - Death*
- *7 - Mechanical ventilation or extracorporeal membrane oxygenation (ECMO), vasopressor support, dialysis/renal replacement therapy (RRT)*
- *6 - Intubation with mechanical ventilation, a mask with a reservoir or oxygen with high-flow nasal goggles.*
- *5 - Noninvasive ventilation (continuous positive airway pressure [CPAP] or bilevel positive airway pressure [BiPAP]) or high-flow oxygen*
- *4 - Oxygen by mask or nasal*
- *3 - Hospitalized with no oxygen therapy*
- *2 - Limitation of activity*
- *1 - Infected without limitations*
- *0 - No clinical or virologic evidence of COVID-19 infection*

Higher WHO Severity Score indicates worser conditions.

11.16.5 Subjects Discharged

Subjects will be considered as discharged at all visits after the discharge date. If there is more than one hospitalization for a subject, then the latest hospitalization will be considered.

11.17 Criterion Flags

- Subjects who are alive at the given timepoints with the below mentioned criteria will be flagged as 'Y' in the analysis datasets. All subjects within Per-Protocol and FAS will be flagged irrespective of their disposition status. Any ambiguity in subject status will be considered as failure and flagged as 'N'.

Criterion Flag	Criteria	Other Criteria
Flag 01	Alive on Day 14	Without the following (end date prior to day 14): • Ongoing use of vasopressors • Ongoing intubation/mechanical ventilation

		• New ongoing need for dialysis/renal replacement therapy (RRT)
Flag 02	Alive on Day 7	Without the following (end date prior to day X): • Ongoing use of vasopressors • Ongoing intubation/mechanical ventilation • Ongoing residence in an ICU • New ongoing need for dialysis/renal replacement therapy (RRT)
Flag 03	Alive on Day 14	
Flag 04	Alive on Day 28	
Flag 05	Alive on Day 60	
Flag 06	Alive on Day 90	

- Subjects who were discharged will be flagged 'Y' in the analysis datasets based on the following criteria:

Criterion Flag	Criteria
Flag 07	Discharged on Day 14
Flag 08	Discharged on Day 28
Flag 09	Discharged on Day 60
Flag 10	Discharged on Day 90

If a subject does not meet the given criteria, they will be flagged as 'N'. All subjects within Per-Protocol and FAS will be flagged irrespective of their disposition status.

11.18 Time to Death

Time to Death will be calculated as follows:

- Time to Death = (Date of Death – Date of First IMP) + 1

Subjects without death in the trial will be censored at either the date of withdrawal or the date of last visit, whichever occurs earlier.

11.19 Self-Evident Corrections

In some instances, spelling errors may be corrected in analysis mapping for 'Other, Specify' fields (free text). These will be reconciled and confirmed during clean file meeting.

12 Statistical Analysis

12.1 Subject Disposition

Number of subjects in screened, all-enrolled and randomized Analysis Set, number and percentage for subjects in safety Analysis Set, FAS, per protocol Analysis Set, subjects who completed the study, study duration (days), number of subjects who terminated the study early along with their reasons will be summarized by treatment. Reason for discontinuation will be displayed in the descending order of "Total" column.

Screened and All-enrolled Analysis Set will be presented only for Total columns. All other summaries will be presented by treatment groups. A CONSORT flowchart will also be presented to visualize the flow of disposition.

Note that randomized Analysis Set will be displayed by planned treatment and all other categories will be displayed by actual treatment.

Percentages will not be displayed for screened and all-enrolled Analysis Set. The percentages by treatment group for randomized analysis set will be based on all-enrolled Analysis Set. All other percentages will be based on randomized Analysis Set. Percentages for categories of reason for discontinuation from the study will be based on the number of subjects who discontinued from the study.

In DDP: Table 14.1.1.1, Figure 14.1.1.1

Subject disposition information, status of inclusion exclusion criteria, randomization details and subjects excluded from Analysis Set along with reasons will be listed by subject. All derived variable summarized in the tables will also be listed.

In DDP: Listings 16.2.1.1, 16.2.1.2, 16.2.1.3 and 16.2.3.1

12.2 Visit Attendance

Number and percentage of subjects who attended each visit (Screening, Day 1, Day 2, Day 3, Day 7, Day 14, Day 28, Day 60, Early Withdrawal and End of Study) will be summarized by treatment group. Percentages will be based on FAS.

In DDP: Table 14.1.2.1

12.3 Protocol Deviations

Number and percentage of subjects with any deviation and number of deviations will be summarized by treatment. The same will be sub-classified by grade (important/not important) and category (Informed consent deviation, Entry Deviation, Dosing Deviation, Withdrawal Deviation, Operational Deviation, Other, COVID-19 Deviation etc.). Deviation categories will be displayed in descending order of the "Total" column.

Percentages will be based on Randomized Analysis Set.

In DDP: Table 14.1.3.1

Protocol deviations will be listed by subject.

In DDP: Listing 16.2.2.1

12.4 Demographic and Baseline Characteristics

Subject demographics will be summarized by treatment. Categorical and continuous variables will be provided in the same table. The following variables will be presented: age (years), sex, ethnicity, race, height (cm), weight (kg), BMI (kg/m^2), childbearing potential and methods of birth control for the subject as well as the partner. Percentages will be based on the non-missing results within the Analysis Sets. Percentages for Childbearing potential and method of birth control will be based only on female population. Method of birth control for the subject's partner will be based only on the male population reporting birth control.

The summaries will be repeated for all randomized, FAS, per protocol and PK Analysis Sets (as per ICH E3 Guidelines). Note that Safety Analysis Set and FAS are same as per definition; hence, the analysis is not repeated for the Safety Analysis Set.

In DDP: Table 14.1.4.1, 14.1.4.2, 14.1.4.3 and 14.1.4.4

Subject demographics will be listed by subject.

In DDP: Listing 16.2.4.1

12.5 Baseline Characteristics

Descriptive statistics for the baseline diagnostic parameters will be summarized by treatment group. The parameters will include: Temperature (°C), Heart Rate (beats/min), Respiratory Rate (breaths/min), Oxygen Saturation (%), Ferritin, D-Dimer, CRP, and Procalcitonin.

The summaries will be repeated for FAS and per-protocol Analysis Sets. If all the Analysis Sets are same, summary will be presented only for FAS. Note that Safety Analysis Set and FAS are same as per definition; hence, the analysis is not repeated for the safety analysis set.

In DDP: Table 14.1.5.1 and Table 14.1.5.2

Baseline Diagnostic Criteria will be listed by subject.

In DDP: Listing 16.2.4.2

12.6 Medical/Surgical History

Number and percentage of subjects with any medical / surgical history and number of events will be summarized by treatment. The same will be classified by System Organ Class (SOC) and Preferred Term (PT). The SOC and PT will be displayed in the descending order of frequency in "Total". Medical history will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0 or Higher.

Percentages will be based on Safety Analysis Set.

The summary will be presented for medical / surgical history and concurrent diseases separately. History and Concurrent Diseases will be flagged as mentioned in Section 11.10.

In DDP: Tables 14.1.6.1 and 14.1.6.2

Medical/Surgical History will be listed by subject and body system.

In DDP: Listing 16.2.4.3

12.7 Prior and Concomitant Medications

Number and percentage of subjects who have taken any prior / concomitant medication will be summarized by treatment and study period. The same will be classified by Therapeutic Main group (ATC Level 2) and Chemical Subgroup (ATC Level 4). If ATC level 4 is missing, ATC levels 2 or 3 will be used. The therapeutic main group and chemical subgroup will be displayed in the descending order of

frequency in "Total" for Treatment Period. Medications will be coded using the World Health Organization's Drug-Dictionary (WHODrug) version September 2020 or latest.

Percentages will be based on Safety Analysis Set.

The summary will be presented for prior and concomitant medications separately. Prior and concomitant medications will be flagged as mentioned in section 11.11.

In DDP: Tables 14.1.7.1 and 14.1.7.2

All medications will be listed by subject and therapeutic subgroup. Prior and concomitant medications will be flagged. Subjects will be grouped by treatment.

In DDP: Listing 16.2.4.4

12.8 Extent of Exposure

Number and percentage of subjects exposed to treatment over time (1st dose, 2nd dose, and 3rd dose), cumulative planned IV to be administered (mL), cumulative actual IV administered (mL), % compliance, and number and percentage of subjects with dose interruptions for each dose (1st dose, 2nd dose, and 3rd dose) along with reason for interruptions will be summarized by treatment. Both continuous and categorical summary will be presented in the same table. Percentages will be based on FAS. Percentages for reason for interruptions will be based on the number of subjects whose dose was interrupted in the respective dose.

In DDP: Table 14.1.8.1

IV administration data will be listed by subject for FAS. Subjects will be grouped by treatment.

In DDP: Listing 16.2.5.1

12.9 Efficacy Analyses

All efficacy analyses will be based on FAS. Analyses will be repeated for Per-Protocol Analysis Set to check the robustness of the results (sensitivity analyses).

12.9.1 Primary Efficacy analysis

12.9.1.1 Proportion of Subjects Alive on Day 14

Number and percentage of subjects alive on Day 14 without the following will be summarized. Percentages will be based on the corresponding analysis set. Subjects who discontinued from the study early or whose survival status is inconclusive on Day 14 will be considered as failure (Not Alive).

- Ongoing use of vasopressors
- Ongoing intubation/mechanical ventilation
- New ongoing need for dialysis/renal replacement therapy (RRT)

The proportion of subjects alive will be compared across treatment arms using a Cochran-Mantel-Haenszel (CMH) method. The common Risk Difference along with associated 80% CI will be reported. Unadjusted p-value for testing the null hypothesis that there is no strong correlation between treatment and subject status will also be reported. As this is a pilot Phase 2 proof-of-concept (POC) trial in an infection with no approved therapy and false negative error (100% minus power) is equally as important as false positive error, the one-sided type 1 error is set at 0.2.

Reference SAS Program:

```
proc freq data=<input> ;
    tables <status>*<treatment> / cmh riskdiff(common) alpha=0.2;
run;
```

The analyses will be based on FAS and repeated for Per-Protocol Analysis Set.

In DDP: Tables 14.2.1.1 and 14.2.1.2, Listing 16.2.6.2, 16.2.6.3, and 16.2.6.4

12.9.2 Secondary Efficacy Analyses

12.9.2.1 Change in WHO Severity Scores

12.9.2.1.1 Shift Summary

Shift in WHO severity scores from baseline (scores 4-6) to each post-baseline visit (Days 2, 3, 7, 14, 28, 60 and 90) will be presented by treatment groups. Subjects whose values are missing or assessment is not done will be presented as 'Missing / Not Done'. Percentages will be based on corresponding population.

In DDP: Tables 14.2.2.1 and 14.2.2.2

12.9.2.1.2 Box Plot

Box plot will be plotted to visualize the trend in average WHO Severity scores at baseline and post-baseline visits (Days 2, 3, 7, 14, 28, 60 and 90). X axis will represent visit and Y axis will represent WHO severity scores. Each treatment group will be plotted in a separate page. Number of subjects at each visit will be annotated below the X-axis.

In DDP: Figures 14.2.2.3 and 14.2.2.4

12.9.2.1.3 MMRM

WHO Severity score change from baseline to each visit will also be analyzed using a mixed model for repeated measures under missing at random framework using WHO scores collected at scheduled visits. Change from baseline to each visit will be specified as the dependent variable. Treatment group, visit, baseline WHO Score and an interaction effect between treatment-by-visit and baseline WHO score-by-visit will be specified as independent variables. Least square estimates of the mean change from baseline and confidence intervals of this estimate will be created for each treatment group by the model. Treatment group will be compared with the Placebo group in a pairwise fashion at each visit.

Further, the difference in the dependent variable between the treatment groups will be estimated for each of these comparisons, as well as 95% confidence intervals for these estimates and p-values

testing the null hypothesis that the difference between the treatment groups is zero. All these hypothesis tests will be made using the same mixed model for repeated measures. The approach allows for the repeated measures within subjects to be taken into account. An unstructured covariance will be assumed to allow the variances and covariances to differ between visits and treatments.

Reference SAS Program:

```
proc mixed data = XXX;
  class trta subjectid visit;
  model chg = trta visit bsl_who trta*visit bsl_who*visit;
  repeated visit / subject=subjectid type=un;
  lsmeans trta*visit / diff cl pdiff;
  lsmeans trta / diff cl pdiff;
run;
```

Reference: Tables 14.2.2.5 and 14.2.2.6

12.9.2.1.4 Listing

WHO Severity scores for all visits will be listed by subject and grouped by treatment groups.

In DDP: Listing 16.2.6.1

12.9.2.2 Time to Death (Days)

12.9.2.2.1 Log-Rank Test

Time-to-event statistics including number of subjects with event (see section 11.18), censored, mean, standard error, median time along with 95% CI, 25th and 75th quartiles, minimum and maximum will be reported in a summary table. Log Rank test will be performed to compare the survival probability curves between treatment groups and corresponding unadjusted p-values will be included.

Percentage of subjects alive at Day 28 and Day 90 will be estimated using Kaplan-Meier method. 95% CI for the point estimate will also be presented.

Reference SAS Program:

```
proc lifetest data = <input> plots=survival;
  time <duration>*<censor>(1);
  strata <treatment>/ test=LOGRANK;
run;
```

12.9.2.2.2 Cox Proportional Model

Cox regression will be performed with WHO Severity score at baseline as continuous covariate in the model to compare hazard between treatment and placebo and to estimate hazard ratio. Hazard Ratio along with 95% CI will be reported in the same table mentioned in section 12.9.2.2.1.

Reference SAS Program:

```
proc phreg data=<data> ;
      class treatment;
      model time*status(01) =treatment bsl_who/rl;
```

```
      hazardratio 'Treatment vs Placebo' treatment;
run;
```

In DDP: Tables 14.2.3.1 and 14.2.3.2

12.9.2.2.3 Kaplan-Meier Curve

Time to death will also be analyzed using Kaplan-Meier curves. X-axis will be the time (days) and Y-axis will be the survival probability. Censored values will be represented with symbol '|' and stratified by treatment groups. Number of subjects at risk over time will be annotated below the X-axis.

In DDP: Figures 14.2.3.3 and 14.2.3.4

12.9.2.2.4 Listing

Death Details will be listed by subject.

In DDP: Listing 16.2.7.4

12.9.2.3 Proportion of Subjects Alive on Days 7, 14, 28, 60 and 90

Number and percentage of subjects alive on Days 7, 14, 28, 60 and 90 without the following will be summarized. Percentages will be based on FAS. Subjects who discontinued from the study early or whose survival status is inconclusive on respective day will be considered as failure (Not Alive).

- Ongoing use of vasopressors
- Ongoing intubation/mechanical ventilation
- Ongoing residence in an ICU
- New ongoing need for dialysis/renal replacement therapy (RRT)

The analyses described in Section 12.9.1.1 will be repeated for each day as part of secondary analyses.

In DDP: Tables 14.2.4.1 and 14.2.4.2, Listing 16.2.6.2, 16.2.6.3, 16.2.6.4

12.9.2.3.1 Proportion of Subjects Alive controlling for stratification factor

Additionally, the proportion of subjects alive on Days 7, 14, 28, 60 and 90 will be compared across treatment arms controlling for stratification factor (WHO Severity score at baseline) using a Cochran-Mantel-Haenszel (CMH) method will be reported for each day as mentioned above. The common Risk Difference along with associated 95% CI will be reported. Unadjusted p-value for testing the null hypothesis that there is no strong correlation between treatment and subject status will also be reported.

In DDP: Tables 14.2.4.3 and 14.2.4.4

12.9.2.4 Proportion of Subjects Discharged

Number and percentage of subjects who were discharged on or before Days 14, 28, 60 and 90 will be summarized by treatment group. Proportions within each treatment group along with 95% CI will be

provided using Clopper-Pearson method for each visit. Risk Differences between treatment groups and p-value from testing the null hypothesis that there are no differences between treatment groups will be reported based on Fisher's Exact test. The summary will be based on FAS and repeated for Per-Protocol Analysis Set.

Reference SAS Program:

```
/* 95% CI for binomial (exact Clopper-Pearson) */

proc freq Data=XXX alpha=0.05;
     by treatment;
     tables flag/binomial(level='1' exact);
run;

/* 95% CI for risk difference and p-value from Fisher's test */

proc freq Data=XXX alpha=0.05;
     tables treatment*flag/riskdiff(cl=exact);
     exact riskdiff fisher;
run;
```

In DDP: Tables 14.2.5.1 and 14.2.5.2 and Listing 16.2.6.2

12.9.2.5 Hospitalization due to COVID 19

Number and percentage of subjects re-admitted to an acute-care hospital and subjects who are ongoing hospitalization at Day 14 will be summarized. Descriptive summaries for Duration of COVID-19 illness before hospitalization and cumulative number of hospitalization days will also be summarized.

Number and percentage of subjects who have been to the ICU and subjects who are still in ICU at End of Study will be summarized. Descriptive summary for cumulative number of ICU days will also be summarized.

Number and percentage of subjects who had Intubation / Mechanical Ventilations and subjects who are still in Intubation / Mechanical Ventilations at End of Study will be summarized. Descriptive summary for cumulative number of Intubation / Mechanical Ventilations days will also be summarized.

All summaries will be based on FAS and per-protocol analysis sets. Percentages will be based on the corresponding analysis sets.

In DDP: Table 14.2.6.1 and Table 14.2.6.2

Hospitalization, ICU and Intubation / Mechanical Ventilations will be listed by subject.

In DDP: Listings 16.2.6.2, 16.2.6.3, and 16.2.6.4

12.9.2.6 Comparison of Days in Hospital, ICU and Ventilation

Cumulative number of days for Hospitalization, ICU and Intubation / Mechanical Ventilation will be compared across treatment groups using non-parametric Wilcoxon Rank Sum test. The test will be two-sided with level of significance of 5%. Descriptive summaries of cumulative number of days,

difference in treatment groups, 95% CI and unadjusted p-value will be reported. P-value will be from testing the null hypothesis that mean of cumulative days across treatment groups are same.

Reference SAS Program:

```
proc nparlway data=<data>;
      class <treatment>;
      var <days>;
run;
```

In DDP: Table 14.2.6.3 and Table 14.2.6.4

12.9.3 Other Analyses

12.9.3.1 Arterial Blood Gas Test

Descriptive summary of absolute results and change from baseline for Arterial blood gas test parameters in baseline and post-baseline visits will be summarized by treatment groups. The parameters to be summarized are, pH, pCO_2, pO_2, $\%O_2$ and cmH_2O. The summary will be presented for FAS and per-protocol analysis set.

In DDP: Tables 14.2.7.1 and 14.2.7.2

Absolute results change from baseline, etc. for all parameters will be listed by subject and grouped by treatment and visit.

In DDP: Listing 16.2.6.6

12.9.3.2 Hypotension requiring treatment beyond fluids (Vasopressors)

Number and percentage of subjects who have taken any vasopressors will be summarized by treatment. The same will be classified by Therapeutic Main group (ATC Level 2) and Chemical Subgroup (ATC Level 4). If ATC level 4 is missing, ATC levels 2 or 3 will be used. The therapeutic main group and chemical subgroup will be displayed in the descending order of frequency in "Total". Medications will be coded using the World Health Organization's Drug-Dictionary (WHODrug) version September 2020 or latest.

The summary will be presented for FAS and per-protocol analysis set. Percentages will be based on corresponding analysis sets.

In DDP: Tables 14.2.8.1 and 14.2.8.2

All medications will be listed by subject and therapeutic subgroup. Subjects will be grouped by treatment.

In DDP: Listing 16.2.6.7

12.9.3.3 CURB-65 Score

Shift in CURB-65 scores from baseline (scores 1-5) to each post-baseline visit (Days 3, 7, 14, 28 and 60) will be presented by treatment groups. Subjects whose values are missing or assessment is not done will be presented as 'Missing / Not Done'.

The summary will be presented for FAS and per-protocol analysis set. Percentages will be based on corresponding analysis sets.

In DDP: Tables 14.2.9.1 and 14.2.9.2

CURB-65 scores will be listed by subject and grouped by treatment groups and visits.

In DDP: Listing 16.2.6.8

12.9.3.4 Abbreviated Mental Health Score

Descriptive summaries for the total score and change from baseline to post-baseline visits will be summarized by treatment groups. The summary will be based on FAS and per-protocol analysis set. Percentages will be based on the corresponding analysis sets.

In DDP: Tables 14.2.10.1 and 14.2.10.2

Abbreviated mental health scores will be listed by subjects.

In DDP: Listing 16.2.6.9

12.9.3.5 Sputum Microbiology, Blood cultures and Dialysis

Sputum microbiology, Blood cultures and Dialysis/RRT data will only be listed by subject.

In DDP: Listing 16.2.6.11, 16.2.6.12 and 16.2.6.5

12.9.3.6 Confirmation of COVID-19 pneumonia

Confirmation of COVID-19 pneumonia by RT-PCR, CXR scan radiologic findings, and CT scan radiologic findings will be listed by subject.

Note: Subject who have screening COVID-19 confirmation before Informed Consent Date will be discussed during the Blinded Review Meeting prior to DB Lock.

In DDP: Listing 16.2.6.10

12.9.4 Pharmacodynamic Parameters

Descriptive summary of parameters for baseline, each post baseline visit, and change from baseline at each visit and time point will be presented by treatment group. The summary will be based on FAS analysis set. The decision on whether biomarker results will be analyzed, and list of biomarkers to be analyzed will be made after database lock.

All PD parameters will be listed for FAS analysis set.

In DDP: Table 14.4.1.1 And Listing 16.2.10.1

12.9.5 Plasma Concentration

12.9.5.1 Continuous Summary

Descriptive summaries including geometric mean and SD, co-efficient of variation (%), geometric co-efficient of variation (%) of plasma concentrations will be presented by gender, time point and treatment groups. The summary will be based on PK analysis set.

All plasma concentration results will be listed by subject for PK analysis set.

In DDP: Table 14.5.1.1, Listing 16.2.10.2

12.9.5.2 Plasma Concentration Time Plots

Drug concentration profiles will be generated as follows:

- Mean Plasma concentration vs time will be presented for subjects within each treatment group along with error bars. Each group will be differentiated by color and symbol with appropriate legend. Y axis will be plasma concentration in ng/mL and X axis will be timepoints in hours. X axis will be displayed linearly proportionate to the actual timepoints.
- Log transformed plots will also be presented for the mean plots.

In DDP: Figures 14.5.1.2 and 14.5.1.3

12.9.6 Pharmacokinetic Parameters

The following PK parameters will be derived from plasma concentration using Phoenix WinNonLin software version 8.3 or higher for each measured analyte:

- Area under the plasma concentration-time curve from time of dosing (zero) to time t of the last measured concentration above the limit of quantification (AUC_{0-t})
- Area under the plasma concentration-time curve (AUC) from 0 to infinity (AUC_{0-inf})
  elimination half-life ($t_{1/2}$)
- Observed maximum plasma concentration (C_{max})
- Time to observed maximum plasma concentration in plasma (T_{max})
- Elimination half-life ($t_{1/2}$)

12.9.6.1 Continuous Summary

Descriptive summaries including geometric mean and SD, co-efficient of variation (%), geometric co-efficient of variation (%) of PK parameters will be presented by gender and treatment group. The summary will be based on PK analysis set.

All PK parameters will be listed for PK analysis set.

In DDP: Table 14.5.1.6, Listing 16.2.10.3

12.9.7 Immunogenicity

Number and percentage of subjects for presence of antibodies against rhu-pGSN will be summarized by treatment and visit. Percentages will be based on the FAS analysis set.

All Immunogenicity parameters will be listed for FAS analysis set.

In DDP: Table 14.6.1.1 and Listing 16.2.10.4

12.10 Safety Analyses

12.10.1 rse Events

All Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) version 23.0 or Higher. All summaries will be based on Safety analysis set.

12.10.1.1 Overall Adverse Events

Number and percentage of subjects and number of events will be summarized by treatment for the following categories:

1. All adverse events reported
2. Treatment emergent adverse events (TEAEs)
3. Serious TEAEs
4. Related TEAEs
5. Related Serious TEAEs
6. Adverse events led to death
7. Adverse events led to study discontinuation
8. Grade 3 or higher TEAEs
9. Grade 3 or higher related AEs
10. Adverse events by severity
11. Injection related Adverse Events by Severity
12. Adverse events by relationship to IMP
13. Adverse events by relationship to study procedure
14. Adverse events by outcome
15. Adverse events by action taken with treatment

Severity grading is based on NCI CTCAE, version 5.0. Percentages will be based on Safety analysis set. If a subject has multiple occurrences with different intensity/ relationships, then all the occurrences will be counted.

In DDP: Table 14.3.1.1

All adverse events will be listed by subject and system organ class. Adverse events will be grouped by subjects. Day the Adverse event started, and Duration of AEs will also be included in the listing.

In DDP: Listing 16.2.7.1

12.10.1.2 Summary of Treatment Emergent Adverse Events by SOC and PT

Number and percentage of subjects and number of adverse events will be summarized by treatment, system organ class and preferred terms. Percentages will be based on safety analysis set. Events will be displayed in the descending order of frequency in "Total".

The same will be repeated for treatment-emergent related AEs, treatment-emergent serious AEs, treatment-emergent related serious AEs. Serious AEs and Deaths will be listed separately for respective sections in CSR (as per ICH E3).

In DDP: Tables 14.3.1.2 to 14.3.1.8, Tables 14.3.2.1 and 14.3.2.2

12.10.1.3 Summary of Adverse Events by Relationship and Intensity

Number and percentage of subjects and number of events in each system organ class, preferred term and intensity (Grade 1-5) will be summarized by relationship for treatment-emergent adverse events and treatment. System organ class and preferred term will be displayed by descending order of frequency in "Total". Intensity will be displayed in the alphabetical order.

In DDP: Table 14.3.1.9

12.10.2 Summary of Death

Number and percentage of deaths due to any cause, AE leading to Death by preferred term, Death due to COVID-19 (WHO score = 8) by visit will be summarized by treatment groups. Percentages are based on Safety analysis set.

In DDP: Table 14.3.2.3

12.10.3 aboratory Assessments

12.10.3.1 Continuous Summary

Descriptive summary of absolute result and change from baseline in laboratory data will be presented by parameter and visit for safety analysis set. Each category (Hematology, Clinical Chemistry and Coagulation) will be represented in separate tables. Note that Laboratory assessments will be done only if required by SOC.

In DDP: Tables 14.3.4.1, 14.3.4.2, and 14.3.4.3

12.10.3.2 Categorical Summary

Number and percentage of subjects reporting laboratory interpretations (Normal, Abnormal Not CS and Abnormal CS, Not Done, Not required as per SOC) will be summarized by treatment, parameter, and visit. Each category (hematology, clinical chemistry, and coagulation) will be represented in separate tables. Percentages will be based on number of subjects with non-missing results in each visit within safety analysis set.

In DDP: Tables 14.3.4.4, 14.3.4.5 and 14.3.4.6

12.10.3.3 Listings

All laboratory results will be listed for all subjects by visit and parameter. Out of range results will be highlighted.

In DDP: Listings 16.2.8.1, 16.2.8.2 and 16.2.8.3

Subjects with clinically significant laboratory results and subjects with out-of-range results will be separately listed by category, visit and parameter.

In DDP: Listings 16.2.8.4, Table 14.3.4.7

HIV and Pregnancy tests will only be listed by subject.

In DDP: Listing 16.2.8.5 and 16.2.8.6

Parameters collected in each laboratory category are listed below. In summaries and listings, parameters will be sorted in the order as below:

Category	Parameters
Hematology	Hemoglobin, Hematocrit, RBC, WBC, Platelet Count, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils, Reticulocyte Count,
Clinical Chemistry	Albumin, Alkaline Phosphatase, Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), Bicarbonate, Direct Bilirubin, Total Bilirubin, Blood Urea Nitrogen, Lactate Dehydrogenase (LDH), Chloride, Creatine Phosphokinase (CPK), Creatinine, Amylase, Lipase, Potassium, Total Protein, Sodium, Ferritin, D-dimer, CRP, Procalcitonin, Urea, Total cholesterol (TC), HDL-C, LDL-C, Triglycerides
Coagulation	PT, PTT, aPTT, International Normalized Ratio (INR)

12.10.4 Other Safety Analyses

12.10.4.1 Vital Signs

Descriptive summary of absolute result and change from baseline in vital signs will be presented by treatment, parameter and visit for Safety analysis set. Parameters to be included: Weight (kg), BMI (kg/m^2), Systolic Blood Pressure (mmHg), Diastolic Blood Pressure (mmHg), Respiratory rate (breaths/min), Heart rate (beats/min) and Temperature (°C). In summaries and listings, parameters will be sorted in the order mentioned.

In DDP: Table 14.3.5.1

Vital signs will be listed by subjects and visit for safety analysis set.

In DDP: Listing 16.2.9.1

12.10.4.2 Physical Examination

Number and percentage of subjects with results (Normal, Abnormal Not CS, Abnormal CS, Not Done) will be summarized by treatment, body system and visit. Body systems to be summarized are: Skin, HEENT, Neurologic, Lungs, Abdomen, and Heart. Percentages will be based on safety analysis set. Any additional body systems assessments as 'Other' will be listed and not summarized.

In DDP: Table 14.3.5.2

Physical Examination will be listed by subject and visit.

In DDP: Listing 16.2.9.2

12.10.4.3 Electrocardiogram Assessments

Descriptive summary of absolute result and change from baseline in EKG Results will be presented by treatment, parameter and visit for Safety analysis set. The parameters to be presented are: Heart Rate (beats/min), PR (msec), RR (sec), QRS (msec), QT (msec) and QTcF (msec). Note that EKG assessment will be done only if required by SOC.

Number and percentage of subjects with findings (Normal, Abnormal Not CS, Abnormal CS, Not Done, Not Required as per SOC) will be summarized by treatment, parameter, and visit. Percentages will be based on safety analysis set.

In DDP: Table 14.3.5.3 and Table 14.3.5.4

EKG Findings will be listed by subject and visit.

In DDP: Listing 16.2.9.3

12.10.5 Exploratory Analyses

Exploratory analyses looking at biomarkers and outcomes in each treatment arm will be conducted. The decision on whether biomarker results will be analyzed, and list of biomarkers to be analyzed will be made after database lock.

13 Changes to Planned Analyses

- One of the Secondary Efficacy Endpoints as per protocol is "Daily change in 9-point WHO severity score through at least Day 14". Since the WHO Severity Score is required only on Days 1, 2, 3, 7 and 14 (on other days, it is not mandatory), the analysis of the WHO Severity score will be done for "Change in 9-point WHO severity score through Day 14 on scheduled visits". All WHO Severity scores will be listed.

- Exploratory analysis to compare the efficacy endpoint data from the rhu-pGSN group from this study to that of external control data was not considered feasible at the time of database lock, so this analysis will not be performed.

14 Index of Tables, Listings and Graphs

Refer BTI_Data Display Plan (Ver: 1.00) for the list of Tables, Listings and Graphs.

15 References

Provide list of references used to create this document.

- ICH. ICH Harmonized Tripartite Guideline: Statistical Principles for Clinical Trials E9. 1998.
- ASA. Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics. 1999.
- ICH. ICH Harmonized Tripartite Guideline: Structure and Content of Clinical Study Reports E3. 1995.
- BTI-201 CSR v1.0 Final 24Dec2019_signed (Phase 1 study protocol)
- BTI-201-Statistical-Anal-PF-v2-Amen-1_2018-12-03 (Phase 1 study SAP)
- CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials

16 Appendices

16.1 Summary of Statistical Analyses

Endpoints	Analysis Set	Primary Analyses	Supportive Analyses
Incidence of SAEs in rhu-pGSN vs placebo groups	Safety analysis set	Descriptive Summaries	-
Proportion of subjects alive not on vasopressors, mechanical ventilator, and dialysis on Day 14.	FAS (primary), Per-Protocol analysis set	Cochran-Mantel-Haenszel (CMH) method	-
Adverse Events, Clinically Significant Laboratory Results	Safety analysis set	Descriptive Summaries	-
Change in WHO Severity Score	FAS, Per-Protocol analysis set	Shift summaries, Box Plots, MMRM	-
Mortality Rate and Time to Death	FAS (primary), Per-Protocol analysis set	Log Rank Test, Cox Regression Model, Kaplan-Meier Curve	-
Proportion of Subjects alive without support	FAS (primary), Per-Protocol analysis set	CMH	-
Days on the Ventilator	FAS (primary), Per-Protocol analysis set	Descriptive Summaries, Wilcoxon Rank Sum Test	-
Hospitalization and ICU days	FAS (primary), Per-Protocol analysis set	Descriptive Summaries	-
Plasma Concentration	PK analysis set	Descriptive Summaries and Plots	
PK Parameters	PK analysis set	Descriptive Summaries	-
Immunogenicity	PK analysis set	Descriptive Summaries	-
Biomarkers	Safety analysis set	Descriptive Summaries	-

17 Change Log

Version	Authored by	Change Date	Change Details	Reviewed by	Review Date
1.00	Bharathy Prasath Shweta Padmanaban	05-Aug-2021	First version approved	Mark DiNubile	05-Aug-2021