Protocol J2X-MC-PYAJ

# A prospective cohort study to evaluate the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 at high risk for progressing to severe illness, with matched controls.

NCT04701658

Approval Date: 18-Dec-2020

# Title Page



**Protocol Title:**

A prospective cohort study to evaluate the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 at high risk for progressing to severe illness, with matched controls

**Protocol Number: J2X-MC-PYAJ**

**Compound(s):** bamlanivimab (LY3819253)

**Study Phase: 2**

**Short Title:** A prospective cohort study to evaluate the effectiveness in the real-world setting of bamlanivimab in participants with mild-to-moderate COVID-19 at high risk for progressing to severe illness, with matched controls

**Sponsor Name:** Eli Lilly and Company

**Legal Registered Address:** Indianapolis, Indiana, USA 46285

**Regulatory Agency Identifier Number(s):**

IND: 150440

**Approval Date:** Protocol Electronically Signed and Approved by Lilly on date provided below.

Approval Date: 18-Dec-2020 GMT

**Medical Monitor Name and Contact Information will be provided separately.**

## Table of Contents

# 1. Protocol Summary

## 1.1. Synopsis

**Protocol Title:** A prospective cohort study to evaluate the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 at high risk for progressing to severe illness, with matched controls

**Rationale:**

This study aims to characterize the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 in adults and adolescents (age ≥12) who are at high risk of progressing to severe COVID-19 and/or hospitalization compared to a similar control population.

**Objectives and Endpoints:**

| Objectives | Endpoints |
|---|---|
| **Primary** | |
| • To determine the proportion of patients with COVID-related hospitalization or death by 29 days among bamlanivimab-treated participants compared to external controls. | • Proportion (percentage) of participants who experience COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death by Day 29 |
| **Secondary** | |
| • To determine the proportion of patients with COVID-related hospitalization up to 60 and 90 days among bamlanivimab-treated participants compared to external controls. | • COVID-19-related hospitalization, defined as ≥24 hours of acute care, up to Days 60 and 90 |
| • To determine the proportion of patients with a COVID-related ED visit through Days 29, 60, and 90. | • ED visits for COVID-related causes |
| • To describe the safety of bamlanivimab-treated participants through Days 29, 60, and 90. | • Adverse events or serious adverse events |

Abbreviation: ED = emergency department.

**Overall Design:**

An open-label, single-arm, prospective, cohort study using matched real-world external controls. There is no placebo arm.

**Design Outline**

***Screening***

Interested participants or their legally authorized representative will sign the appropriate informed consent and child/adolescent assent document(s), as appropriate, prior to completion of any procedures.

The investigator will confirm a positive RT-PCR test or antigen testing confirmation for COVID-19 (if antigen test is accompanied by symptoms suggestive of SARS-CoV-2 infection), and review criteria for high risk under the EUA to confirm eligibility.

***Treatment and Assessment Period***

This is the general sequence of events during the treatment and assessment period:

- complete baseline procedures to confirm eligibility per inclusion and exclusion criteria and high-risk criteria per EUA
- participants receive infusion of bamlanivimab, and
- complete all safety monitoring and post-infusion data collection.

This table describes the visit types

| **Study Day** | **Visit Type** |
|---|---|
| 1 | Bamlanivimab infusion at site |
| 24 hours (+1 day) | Telephone contact |
| 29(±5 days), 60 (±7 days), 90 (±7 days) | EMR review and/or phone call |
| Early discontinuation and follow-up | Telephone contact |

If a participant is hospitalized, procedures and assessments will continue per the SoA.

This table describes discharge from hospital scenarios if an outpatient is subsequently hospitalized.

***Discharge from Hospital (Outpatients Subsequently Hospitalized)***

| **If hospital discharge…** | **Then…** |
|---|---|
| Occurs prior to Day 29 | Participants will be asked to complete the remaining study assessments at the timepoints indicated in the SoA. |
| Occurs on the same day as a study assessment visit | Assessments do not need to be repeated if the study assessments occurred within 8 hours of discharge and there has been no change in clinical status and the information is available to the site. |
| Does not occur at or prior to Day 28 | Assessments will continue to occur up to Day 90 or until hospital discharge, whichever is later. |

***Post-treatment Follow-Up***

Post-infusion follow-up assessments will be conducted at Days 2, 28, 60, and 90 to assess clinical status and for adverse events.

**Disclosure Statement**: This is a treatment study.

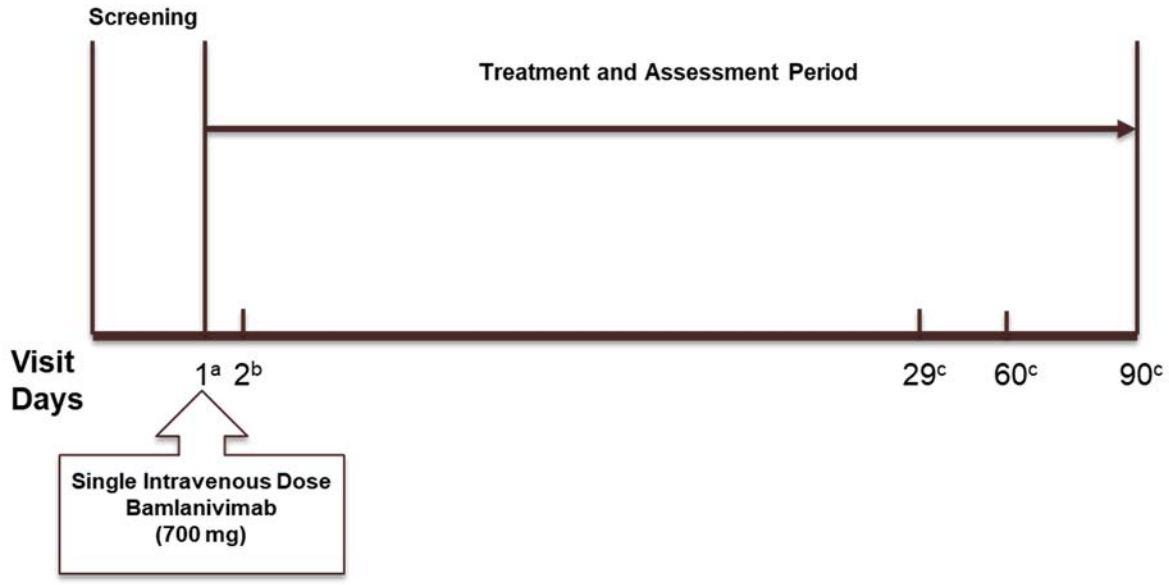
**Number of Participants:**

The initial plan is to enroll up to 3000 participants in the treated cohort over 4-6 weeks of enrollment, with the same number in the control cohort.

**Data Monitoring Committee:** No

## 1.2. Schema

The following figure illustrates the study design for participants receiving bamlanivimab.




[a] Screening and Day 1 procedures may occur on the same day.

[b] Telephone call 24 hours post-infusion.

[c] EMR review and/or phone call.

**Note:** Matched controls will include NM Health Members who have EMR and claims data to determine positive COVID test and any subsequent healthcare utilization, including hospitalization and death data, to determine meeting of entry criteria such as mild/moderate symptoms.

## 1.3. Schedule of Activities (SoA)

Visits may be conducted as a telephone call or EMR review, as long as the protocol SoA is followed. Refer to the study day and visit type table in Section 4.1 for additional clarification.

This SoA is for participants receiving bamlanivimab only.

| **Study J2X-MC-PYAJ** | **Screen** | **Infusion Day** | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Study Day** | | **1** | **2** | **29** | **60** | **90** | **ED** | Screening and Day 1 procedures may occur on the same day.<br>Day 2 = telephone call 24 hours post-infusion<br>Day 29, 60, 90 = EMR and/or telephone call review as necessary |
| **Visit Window (± number of days)** | | -- | 2* | 5 | 7 | 7 | | Visits may not be combined.<br>*Day 2 call visit window +2 only |
| **Procedures** | | | | | | | | |
| Informed consent | X | | | | | | | |
| Inclusion and exclusion criteria review | X | | | | | | | |
| Demographics | X | | | | | | | Including age, gender, race, ethnicity |
| Preexisting conditions and medical history | X | | | | | | | Obtained from interview or available information.<br>Includes timing of exposure and onset of symptoms suggestive of SARS-CoV-2 infection, and risk factors and comorbidities associated with severe COVID-19 illness. |
| Height | | X | | | | | | |
| Weight | | X | | | | | | |
| Prior treatments of special interest within the last 30 days | X | | | | | | | NSAIDs, antivirals, antibiotics, anti-malarials, corticosteroids, immunomodulators, or other investigational treatments. |
| Tobacco use | X | | | | | | | |
| Concomitant medications | | X | X | X | X | X | | |

| **Study J2X-MC-PYAJ** | **Screen** | **Infusion Day** | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Study Day** | | **1** | **2** | **29** | **60** | **90** | **ED** | Screening and Day 1 procedures may occur on the same day.<br>Day 2 = telephone call 24 hours post-infusion<br>Day 29, 60, 90 = EMR and/or telephone call review as necessary |
| **Visit Window (± number of days)** | | -- | 2* | 5 | 7 | 7 | | Visits may not be combined.<br>*Day 2 call visit window +2 only |
| SAEs/AEs | X | X | X | X | X | X | X | Any events that occur after signing the informed consent are considered SAEs/AEs as defined in Section 10.2.<br><br>Hospitalization, ED visits, and deaths from COVID-19 are captured as endpoints and not as SAEs.<br><br>SAEs/AEs will also be collected at the time of early discontinuation, if applicable. |
| Physical examination | X | | | | | | | |
| Vital signs | | X | | | | | | Includes: body temperature, pulse rate, BP, respiratory rate, SpO2, and supplemental oxygen flow rate, FiO2 if known, and method of delivery, if applicable.<br>Record SpO2 while participant is at rest.<br><br>**Day 1 recommended** timing of vitals:<br>1. immediately before the infusion<br>2. every 15 minutes during the infusion, as possible, and<br>3. every 30 minutes for at least 1 hour after the infusion.<br>During infusion, record pulse rate, BP and SpO2. Automation may be used. See Section 8.2.2 for data collected on CRF. |

| **Study J2X-MC-PYAJ** | **Screen** | **Infusion Day** | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Study Day** | | **1** | **2** | **29** | **60** | **90** | **ED** | Screening and Day 1 procedures may occur on the same day.<br>Day 2 = telephone call 24 hours post-infusion<br>Day 29, 60, 90 = EMR and/or telephone call review as necessary |
| **Visit Window (± number of days)** | | -- | 2* | 5 | 7 | 7 | | Visits may not be combined.<br>*Day 2 call visit window +2 only |
| Hospitalization events | | X* | X | X | X | X | X | *Post-infusion only (otherwise exclusion criterion)<br>Record if the following events occur or occurred since prior visit:<br>• Emergency room visits<br>• hospitalized<br>• ICU admittance,<br>• Extended care facility admittance, and<br>• Discharge |
| Death | | X | X | X | X | X | X | From COVID-19-related causes |

Abbreviations: AE = adverse event; BP = blood pressure; CRF = case report form; ED = early discontinuation; FiO2 = fraction of inspired oxygen in the air; ICU = intensive care unit; NSAIDS = non-steroidal anti-inflammatory drugs; SpO2 = saturation of peripheral oxygen.

# 2. Introduction

## 2.1. Study Rationale

The efficient community spread of SARS-CoV-2 has resulted in the current pandemic of COVID-19, which in severe and critical cases results in progressive pulmonary infection, complicated by respiratory failure, with a high prevalence of acute respiratory distress syndrome. Although several therapies have been explored in severe COVID-19, none have improved survival, including antivirals, glucocorticoids, and immunoglobulins (Liu et al 2020).

This study aims to characterize the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 in adults adolescents (age ≥12) who are at high risk of progressing to severe COVID-19 and/or hospitalization compared to a similar control population.

## 2.2. Background

The SARS-CoV-2 gains entry to cells through binding of the spike (S) protein to ACE2 receptors on cells (Hoffmann 2020). Eli Lilly and Company has a partnership with AbCellera Biologics Inc. (AbCellera; Vancouver, Canada) to develop neutralizing IgG1 mAbs to the spike (S) protein of SARS-CoV-2 as a potential treatment for COVID-19. Candidate antibody gene sequences have been selected from a recently recovered COVID-19 US patient's serum using AbCellera's core platform screening technologies.

## 2.3. Benefit/Risk Assessment

Anticipated risk is considered low and is based on the known mechanism of action for human-derived neutralizing antibodies in acute viral disease states. A theoretical risk is that this intervention may cause ADE of viral replication. This is based on responses observed to some monoclonal antibody therapies used in other unrelated viral diseases. Unlike ADE associated with dengue and Zika virus infections, this phenomenon has not been clearly established for coronavirus infections, such as SARS and Middle East respiratory syndrome, and has not been reported to date with SARS-CoV-2. Additionally, limited experience with the use of convalescent serum as a treatment for patients with severe COVID-19 disease has not indicated safety concerns (Shen et al. 2020; Duan et al. 2020).

The risk of clinical ADE for either intervention or in combination is considered low due to

- the absence of ADE from in vitro studies, and
- the absence of ADE from in vivo nonhuman primate studies for bamlanivimab.

To date, there is no evidence of productive enhancement of ADE with SARS-CoV-2.

Additional manageable risks associated with most therapeutic monoclonal antibodies are the potential for infusion-related hypersensitivity and cytokine release reactions. The single infusion in this study will be administered at a controlled rate, the study participants will be monitored closely, and adjustments in the infusion rate will be made and/or the infusion stopped, if indicated. Additional information regarding infusion reaction management options is located in Section 6.1.1.2.

Given the totality of data on bamlanivimab, the well-established safety profile of other therapeutic mAbs, and the lack of disease-directed therapeutic options for patients with COVID-19 illness or to prevent the SARS-CoV-2 infection, the overall benefit or risk assessment of this study is considered favorable.

More detailed information about the known and expected benefits and risks and reasonably expected adverse events of bamlanivimab may be found in the IB.

# 3. Objectives and Endpoints

| Objectives | Endpoints |
|---|---|
| **Primary** | |
| • To determine the proportion of patients with COVID-related hospitalization or death by 29 days among bamlanivimab-treated participants compared to external controls. | • Proportion (percentage) of participants who experience COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death by Day 29 |
| **Secondary** | |
| • To determine the proportion of patients with COVID-related hospitalization up to 60 and 90 days among bamlanivimab-treated participants compared to external controls. | • COVID-19-related hospitalization, defined as ≥24 hours of acute care, up to Days 60 and 90 |
| • To determine the proportion of patients with a COVID-related ED visit through Days 29, 60, and 90. | • ED visits for COVID-related causes |
| • To describe the safety of bamlanivimab-treated participants through Days 29, 60, and 90. | • Adverse events or serious adverse events |

Abbreviation: ED = emergency department.

# 4. Study Design

## 4.1. Overall Design

This study is being conducted in the same population as in the Emergency Use Authorization (EUA [FDA 2020a]).

Study J2X-MC-PYAJ is an open-label, single-arm, prospective, cohort study using matched real-world external controls. There is no placebo arm.

**Screening**

Interested participants or their legally authorized representative will sign the appropriate informed consent and child or adolescent assent document(s), as appropriate, prior to completion of any procedures. The participant may enter the study with a previous positive SARS-CoV-2 viral test result from an external testing facility. This test result must be the first time the participant has had a positive RT-PCR or antigen testing confirmation for COVID-19 (if antigen test is accompanied by symptoms suggestive of SARS-CoV-2 infection)for SARS-CoV-2.

Prescreening prior to administration of bamlanivimab may be conducted to collect baseline information.

The investigator will review symptoms, risk factors, and other non-invasive inclusion and exclusion criteria prior to any invasive procedures. If the participant is eligible after this review, then the site will perform the invasive procedures.

**Treatment and Assessment Period**

This is the general sequence of events during the treatment and assessment period:

- complete baseline procedures to confirm eligibility (positive COVID-19 test, high-risk criteria per EUA)
- participants receive study intervention, and
- complete all safety monitoring and post-infusion data collection.

***Treated population visit types***

This table describes the visit types for the treatment population for this study.

| ***Study day*** | ***Activity*** | ***Visit type*** |
|---|---|---|
| Up to 10 days before infusion | Positive COVID-19 test<br><br>Confirm high-risk criteria per EUA | Ambulatory setting |
| 1 | Infusion | Ambulatory setting |
| 2 | AE or SAE data collection (24 hours post-infusion)<br><br>Endpoints including hospitalization or ED visit for COVID-19 | Telephone call |

| | | |
|---|---|---|
| 29 | AE or SAE data collection<br><br>Primary endpoint collection—hospitalization for COVID-19; | EMR and/or telephone call |
| 60, 90 | AE or SAE data collection<br><br>Endpoints including hospitalization or ED visit for COVID-19 | Electronic and/or telephone call |

Abbreviations: AE = adverse event; ED = emergency department; EUA = emergency use authorization; SAE = serious adverse event.

***Guidelines if a participant is hospitalized***

If a participant is hospitalized, procedures and assessments will continue per the SoA (Section 1.3).

This table describes discharge from hospital scenarios if an outpatient is subsequently hospitalized.

| **If hospital discharge…** | **Then…** |
|---|---|
| Occurs prior to Day 29 | Participants will be asked to complete the remaining study assessments at the timepoints indicated in the SoA. |
| Occurs on the same day as a study assessment visit | Assessments do not need to be repeated if the study assessments occurred within 8 hours of discharge, and there has been no change in clinical status and the information is available to the site. |
| Does not occur at or prior to Day 29 | Assessments will continue to occur up to Day 90 or until hospital discharge, whichever is later. |

Abbreviation: SoA = schedule of activities.

**Post-treatment follow-up**

Post-treatment follow-up assessments will be conducted at Days 2, 29, 60, and 90 to assess study endpoints.

## 4.2. Scientific Rationale for Study Design

**Overall Design**

This study is designed to characterize the real-world effectiveness of bamlanivimab in participants with mild-to-moderate COVID-19 in adults and children who are at high risk of progressing to severe COVID-19 and/or hospitalization compared to a similar control population.

**Participant Characteristics**

The participant population are those infected with SARS-CoV-2 who are at high risk of developing severe disease requiring hospitalization. There is historical evidence that patients infected with upper respiratory viruses who are treated early in their disease course have better responses to anti-viral therapies (Aoki et al., 2003); all patients in the treated cohort will receive an infusion of bamlanivimab within 10 days of their positive COVID-19 test.

The population of participants with mild-to-moderate COVID-19 illness who are at high risk of developing severe disease per the EUA was chosen to evaluate if effective antiviral antibody therapy may prevent progression to the severe form of COVID-19 illness by treating this population early in their disease course and prior to respiratory compromise and failure.

Participants with these risk factors are at higher risk for more severe disease and hospitalization. This population was chosen to evaluate if effective antiviral antibody therapy may prevent hospitalization or death.

## 4.3. Justification for Dose

Bamlanivimab-700 mg was estimated as the maximum therapeutic dose based on PK/PD viral dynamics modeling of Study J2W-MC-PYAB and has a sustained concentration above the in vitro IC90 of viral cell-entry neutralization in the lung tissue (95th percentile of the estimates used) for at least 28 days in 90% of the participant population.

## 4.4. End of Study Definition

A participant is considered to have completed the study if they have completed all required phases of the study including the last scheduled procedure shown in the SoA (Section 1.3).

The end of the study is defined as the date of last scheduled procedure shown in the SoA (Section 1.3) for the last participant in the trial.

# 5. Study Population

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

Due to the criticality of participant health, verbal interview of the potential participant, or their legal representative or family member, may be the source for disease characteristics and medical history, unless otherwise specified within the eligibility criteria.

## 5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

**Age**

1. Are ≥12 years of age at the time of screening

**Disease Characteristics**

2. Are currently not hospitalized
3. Have one or more mild or moderate COVID-19 symptoms (FDA resource page, available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-developing-drugs-and-biological-products-treatment-or-prevention)
    i. Fever
    ii. Cough
    iii. Sore throat
    iv. Malaise
    v. Headache
    vi. Muscle pain
    vii. Gastrointestinal symptoms, or
    viii. Shortness of breath with exertion
4. Must have first positive SARS-CoV-2 viral infection determination and as soon as possible within 10 days of symptom onset
5. Are males or non-breastfeeding females
   Reproductive and Contraceptive agreements and guidance is provided in Section 10.3, Appendix 3. Contraceptive use by males or females should be consistent with local regulations for those participating in clinical studies

**Study Procedures**

6. Understand and agree to comply with planned study procedures

**Informed Consent**

7. The participant or legally authorized representative gives signed informed consent and/or assent as described in Section 10.1.3, which includes compliance with the requirements and restrictions listed in the ICF and in this protocol

**High risk as defined per EUA fact sheet:** https://www.fda.gov/media/143603/download

8. For example, participants who meet at least 1 of the following criteria:

    - Have a BMI ≥35
    - Have chronic kidney disease
    - Have diabetes
    - Have immunosuppressive disease
    - Are currently receiving immunosuppressive treatment
    - Are ≥65 years of age
    - Are ≥55 years of age AND have
        - cardiovascular disease, OR
        - hypertension, OR
        - chronic obstructive pulmonary disease or other chronic respiratory disease.
    - Are 12–17 years of age AND have
        - BMI ≥85th percentile for their age and gender based on CDC growth charts, https://www.cdc.gov/growthcharts/clinical_charts.htm, OR
        - sickle cell disease, OR
        - congenital or acquired heart disease, OR
        - neurodevelopmental disorders, for example, cerebral palsy, OR
        - a medical-related technological dependence, for example, tracheostomy, gastrostomy, or positive pressure ventilation (not related to COVID-19), OR
        - asthma, reactive airway or other chronic respiratory disease that requires daily medication for control.

## 5.2. Exclusion Criteria

Limitations of Benefit and Potential for Risk in Patients with Severe COVID-19

Benefit of treatment with bamlanivimab has not been observed in patients hospitalized due to COVID-19. Monoclonal antibodies, such as bamlanivimab, may be associated with worse clinical outcomes when administered to hospitalized patients with COVID-19 requiring high flow oxygen or mechanical ventilation.

More specifically, participants are excluded from the study if any of the following criteria apply:

**Medical Conditions**

9. Participants who:
    a. are hospitalized due to COVID-19, OR

   b. require oxygen therapy due to COVID-19, OR
   c. require an increase in baseline oxygen flow rate due to COVID-19 in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity.
10. Have SpO2 ≤ 90% on room air or PaO2/FiO2 < 300, respiratory rate ≥30 per minute, heart rate ≥125 per minute (FDA resource page, available at: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/covid-19-developing-drugs-and-biological-products-treatment-or-prevention)
11. Have body weight <40 kg.
12. Require mechanical ventilation or anticipated impending need for mechanical ventilation
13. Have known allergies to any of the components used in the formulation of the interventions
14. Suspected or proven serious, active bacterial, fungal, viral, or other infection (besides COVID-19) that in the opinion of the investigator could constitute a risk when taking intervention
15. Have any comorbidity requiring surgery within <7 days, or that is considered life-threatening within 29 days
16. Have any serious concomitant systemic disease, condition, or disorder that, in the opinion of the investigator, should preclude participation in this study

**Other Exclusions**

17. Have a history of a positive SARS-CoV-2 serology test
18. Have a history of a positive SARS-CoV-2 test prior to the one serving as eligibility for this study
19. Have received an investigational intervention for SARS-CoV-2 prophylaxis within 30 days before dosing
20. Have received treatment with a SARS-CoV-2-specific monoclonal antibody, remdesivir, or other treatment for COVID-19
21. Have received convalescent COVID-19 plasma treatment
22. Have participated in a previous SARS-CoV-2 vaccine study
23. Have participated, within the last 30 days, in a clinical study involving an investigational intervention. If the previous investigational intervention has a long half-life, 5 half-lives or 30 days, whichever is longer, should have passed.
24. Are concurrently enrolled in any other type of medical research judged not to be scientifically or medically compatible with this study
25. Are breast-feeding
26. Are investigator site personnel directly affiliated with this study, and

## 5.3. Matched controls

Matched controls will include NM Health System members who have EMR and claims data to determine positive COVID test and any subsequent healthcare utilization, including hospitalization and death data. Data for control participants will indicate that that they are similar to treated participants according to COVID-19 symptoms and other study entry criteria. If applicable, non-NM Health System members may be used as members of the control

population based on EMR review and matching to enrolled participants. A waiver of informed consent and HIPAA authorization will be requested for matched controls.

## 5.4. Lifestyle Considerations

Reproductive and Contraceptive guidance is provided in Section 10.3, Appendix 3.

## 5.5. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently enrolled in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the Consolidated Standards of Reporting Trials publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAE.

Individuals who do not meet the criteria for participation in this study (screen failure) may not be rescreened.

# 6. Study Intervention

Study intervention is defined as any investigational intervention(s), marketed product(s), placebo, or medical device(s) intended to be administered to/used by a study participant according to the study protocol.

## 6.1. Study Intervention(s) Administered

Each participant will receive a single IV infusion of bamlanivimab.

Study intervention must be administered within 10 days of symptom onset and following the first positive SARS-CoV-2 test sample collection.

| | |
|---|---|
| **Intervention name** | Bamlanivimab (LY3819253) |
| **Dose formulation** | Solution |
| **Dosage level (mg)** | 700 |
| **Use** | Experimental |
| **IMP and NIMP** | IMP |
| **Sourcing** | From Lilly |
| **Packaging and labeling** | Study intervention will be provided in glass vials and will be labeled appropriately |

Abbreviations: IMP = investigational medicinal product; IV = intravenous; NIMP = non-investigational medicinal product.

Infusion information may be found in the pharmacy manual.

The infusion rate may be reduced as deemed necessary if an infusion reaction is observed (Section 6.1.1.2). Participants will be monitored for at least 1 hour after completion of the infusion.

The site must have age-appropriate resuscitation equipment, emergency drugs, and appropriately training staff available during the infusion and for at least 1 hour after the completion of the infusion.

Self-isolation procedures should be followed per local guidelines.

### 6.1.1. Special Treatment Considerations

#### 6.1.1.1. Premedication for Infusions

Premedication for infusions is not planned. However, if an infusion reaction occurs during administration or if the participant has a medical history suggesting a potential benefit from premedication, the study investigator(s) should determine the appropriate premedication. The investigators and sponsor may decide to use premedication if the frequency of infusion reactions among participants warrants it.

If minor infusion reactions are observed, administration of acetaminophen, 500 to 1000 mg, antihistamines, and/or other appropriately indicated medications may be given prior to the start of infusions for subsequent participants.

The decision to implement premedication for infusions in subsequent participants will be made by the investigator and sponsor and recorded in the study documentation.

Any premedications given will be documented as a concomitant therapy.

#### 6.1.1.2. Management of Infusion Reactions

Access to medications (e.g., epinephrine, norepinephrine, steroids, and diphenhydramine) for potential anaphylaxis and serious infusion reactions is mandatory at all infusion sites.

**Symptoms and Signs**

Symptoms and signs that may occur as part of an infusion reaction include, but are not limited to, fever, chills, nausea, headache, bronchospasm, hypotension, angioedema, throat irritation, rash including urticaria, pruritus, myalgia, and dizziness.

Infusion-related reaction severity will be assessed and reported using the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1 (July 2017).

This table describes the severity of reactions according to DAIDS.

| Parameter | Mild | Moderate | Severe | Severe and Potentially Life-threatening |
|---|---|---|---|---|
| Acute Allergic Reaction | Localized urticaria (wheals) with no medical intervention indicated | Localized urticaria with intervention indicated<br>OR<br>Mild angioedema with no intervention indicated | Generalized urticaria<br>OR<br>Angioedema with intervention indicated<br>OR<br>Symptoms of mild bronchospasm | Acute anaphylaxis<br>OR<br>Life-threatening bronchospasm<br>OR<br>Laryngeal edema |
| | | | | |

Source: DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, Version 2.1 (July 2017).

### 6.1.2. Temporary Stopping Criteria

A study sponsor representative and/or study medical monitor will review evolving unblinded safety data to determine if any changes should be made to study conduct.

This table describes the location of AE-related information in this protocol.

| Topic | Location |
|---|---|
| DAIDS table describing severity of reactions | Section 6.1.1.2 |
| Definition of AEs | Section 10.2.1 |
| Assessment of intensity or severity | Section 10.2.3 |

Abbreviations: AE = adverse event; DAIDS = Division of AIDS.

Changes to the planned dosing schedule must be appropriately documented and communicated with the study personnel and the IRB/IEC before dosing continues.

## 6.2. Preparation/Handling/Storage/Accountability

The investigator or designee must confirm appropriate storage conditions have been maintained during transit for all study intervention received and any discrepancies are reported and resolved before use of the study intervention.

Only participants enrolled in the study may receive study intervention, and only authorized site staff may supply or administer study intervention.

All study intervention must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the investigator and authorized study personnel.

The investigator or designee is responsible for study intervention accountability, reconciliation, and record maintenance (i.e., receipt, reconciliation, and final disposition records).

Further guidance and information for the final disposition of unused study interventions are provided in the pharmacy manual.

## 6.3. Measures to Minimize Bias: Randomization and Blinding

**Propensity Score Matching**

The non-randomized nature of a cohort study introduces the possibility of bias. Therefore, the analysis will use propensity score (PS) matching using risk factors associated with hospitalization for COVID-19. The purpose of PS matching is to create balance in the 2 cohorts on specific relevant covariates. PS will be estimated for each patient in the bamlanivimab group and the comparator cohort by the logistic regression model, with treatment status as the dependent variable and the pre-defined independent variables considered as the potential confounders. The success of the PS is judged by the balance in the confounder distributions it produces between the 2 study groups. Prior to initiating the outcome analysis, the quality of the PS adjustment and associated assumptions will be evaluated. The PS model will be finalized prior to initiating the analysis of the outcome measure. Further details will be provided in the SAP.

## 6.4. Study Intervention Compliance

Participants will receive study intervention directly from the investigator or designee, under medical supervision. The date and time of dosing will be recorded in the source documents and recorded in the CRF. The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site staff other than the person administering the study intervention.

## 6.5. Concomitant Therapy

**Prior Treatment**

Convalescent COVID-19 plasma treatment is not allowed prior to enrollment.

For adolescent participants, record any vaccines received 90 days prior to signing informed consent.

**Concomitant Therapy**

Participants should be treated according to standard of care, even as it evolves, and medications may be part of the treatment paradigm. Therefore, remdesivir, or baricitinib plus remdesivir, may be initiated as standard of care for participants hospitalized with severe disease (if available through the FDA EUAs) if hospitalization occurs following infusion of bamlanivimab.

If the local standard of care per written policies or guidelines (i.e., not just an individual clinician decision) includes lopinavir or ritonavir, chloroquine, hydroxychloroquine, or other investigational agents, then initiating these during the study (after infusion of bamlanivimab) is permitted but may require additional safety monitoring by the site.

Any medication, investigational agent, or vaccine, including over-the-counter or prescription medicines, vitamins, and/or herbal supplements, or other specific categories of interest that the participant is receiving at the time of enrollment or receives during the study must be recorded along with

- reason for use
- dates of administration including start and end dates, and
- dosage information including dose and frequency for concomitant therapy of special interest.

Acetaminophen and corticosteroid use are permitted at any time during the study.

Other concomitant medication may be considered on a case-by-case basis by the investigator in consultation with the sponsor if required.

The sponsor should be contacted if there are any questions regarding concomitant or prior therapy.

## 6.6. Dose Modifications

No dose modifications are planned for this study.

## 6.7. Intervention after the End of the Study

No continued access is planned after completion of this study.

# 7. Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal

Discontinuation of specific sites or that of the trial as a whole are handled as part of regulatory, ethical, and trial oversight considerations in Section 10.1, Appendix 1.

## 7.1. Discontinuation of Study Intervention

In rare instances, it may be necessary for a participant to permanently discontinue study intervention. If the IV infusion is definitively discontinued, the participant will remain in the study for the remainder of the assessment visits through Day 90.

## 7.2. Participant Discontinuation/Withdrawal from the Study

A participant may withdraw from the study

- at any time at his or her own request
- at the request of his or her designee (e.g., parents or legal guardian)
- at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons, and
- if enrollment in any other clinical study involving an investigational product or enrollment in any other type of medical research judged not to be scientifically or medically compatible with this study.

Discontinuation is expected to be uncommon.

At the time of discontinuation, if possible, an early discontinuation phone call should be conducted to ascertain SAEs/AEs, as described in the SoA (Section 1.3).

If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent. If a participant withdraws from the study, they may request destruction of any samples taken and not tested, and the investigator must document this in the site study records.

### 7.2.1. Discontinuation of Inadvertently Enrolled Participants

If the sponsor or investigator identifies a participant who did not meet enrollment criteria and was inadvertently enrolled, then the participant should be discontinued from study intervention unless there are extenuating circumstances that make it medically necessary for the participant to continue study intervention.

If the investigator and the sponsor CRP agree it is medically appropriate to continue, the investigator must obtain documented approval from the sponsor CRP to allow the inadvertently enrolled participant to continue in the study with or without treatment with investigational product.

Safety follow-up is as outlined in

- Section 1.3 (SoA)
- Section 8.2 (Safety Assessments), and
- Section 8.3 (Adverse Events and Serious Adverse Events).

## 7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if he or she repeatedly is unavailable for scheduled visits and is unable to be contacted by the study site. Site personnel or designee are expected to make diligent attempts to contact participants who are unavailable for a scheduled visit or were otherwise unable to be followed up by the site.

Site personnel, or an independent third party, will attempt to collect the vital status of the participant within legal and ethical boundaries for all participants that received study intervention. Public sources may be searched for vital status information. If vital status is determined to be deceased, this will be documented and the participant will not be considered lost to follow-up. Sponsor personnel will not be involved in any attempts to collect vital status information.

# 8. Study Assessments and Procedures

Study procedures and their timing are summarized in the SoA (Section 1.3).

Protocol waivers or exemptions are not allowed.

After signing of informed consent, any immediate safety concerns should be discussed with the sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study intervention. All outlined AE or SAE reporting must be done as applicable.

Adherence to the study design requirements, including those specified in the SoA (Section 1.3), is essential and required for study conduct.

All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Data for this study will be collected from telephone calls and the EMR.

## 8.1. Efficacy Assessments

Hospitalization events (Section 8.2.2) will be used to characterize the primary outcome.

## 8.2. Safety Assessments

Planned time points for all safety assessments are provided in the SoA (Section 1.3).

### 8.2.1. Vital Signs

Vital signs will be measured as specified in the SoA (Section 1.3) at the infusion visit. Vital signs include

- body temperature
- blood pressure
- pulse rate
- respiration rate
- saturation of peripheral oxygen, and
- supplemental oxygen flow rate, FiO2 if known, and method of delivery, if applicable.

Additional vital signs may be measured during the study if warranted, as determined by the investigator.

### 8.2.2. Hospitalization Events

If a participant is admitted to the hospital, the participant will remain in the study and follow the procedures outlined in the SoA (Section 1.3). Hospitalization is defined as ≥24 hours of acute care.

The date of hospitalization events will be recorded in the CRF and includes

- hospitalization

- emergency room visit
- ICU admittance
- extended care facility admittance, and
- discharge.

## 8.3. Adverse Events and Serious Adverse Events

AEs will be reported by the participant, or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative. Hospitalization, ED, visits, and deaths from COVID-19 are captured as endpoints and not as AEs or SAEs (see Section 10.2.1).

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, considered related to the study intervention or study procedures, or that caused the participant to discontinue the study intervention or study.

### 8.3.1. Time Period and Frequency for Collecting AE and SAE Information

All AEs and SAEs will be collected from the time of signing of the ICF until participation in study has ended.

Adverse events that begin before the start of study intervention but after signing of the ICF will be recorded on the Adverse Event CRF.

Although all AEs after signing the ICF are recorded by the site in the CRF/electronic data entry, SAE reporting to sponsor begins after the participant has signed the ICF and has received study intervention. However, if an SAE occurs after signing the ICF, but prior to receiving study intervention, it needs to be reported within the SAE reporting timeframe if it is considered reasonably possibly related to study procedures.

All SAEs will be recorded and reported to the sponsor or designee immediately and under no circumstance should this exceed 24 hours of awareness, as indicated in Section 10.2, Appendix 2. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

Investigators are not obligated to actively seek AEs or SAEs after conclusion of the study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has been discharged from the study, and he or she considers the event to be reasonably related to the study intervention or study participation, the investigator must promptly notify the sponsor.

### 8.3.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AE and SAE and the procedures for completing and transmitting SAE reports are provided in Section 10.2.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and non-leading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

### 8.3.3. Follow-Up of AEs and SAEs

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits or contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3). Further information on follow-up procedures is provided in Section 10.2.

### 8.3.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities towards the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRB/IEC, and investigators.

An investigator who receives an investigator safety report describing an SAE or other specific safety information (e.g., summary or listing of SAEs) from the sponsor will review and then file it with the IB and will notify the IRB/IEC, if appropriate according to local requirements.

### 8.3.5. Pregnancy

Details of all pregnancies in female participants will be collected for 90 days after pregnancy outcome.

If a pregnancy is reported, the investigator should inform the sponsor within 24 hours of learning of the pregnancy and should follow the procedures outlined in Section 10.3, Appendix 3.

Abnormal pregnancy outcomes, for example, spontaneous abortion, fetal death, stillbirth, congenital anomalies, and ectopic pregnancy, are considered SAEs.

### 8.3.6. Hypersensitivity Reactions

Many drugs, but particularly biologic agents, carry the risk of systemic hypersensitivity reactions.

If such a reaction occurs, additional details describing each symptom should be provided to the sponsor in the infusion-related reaction/hypersensitivity CRF.

Sites should have appropriately trained medical staff and appropriate medical equipment available when study participants are receiving intervention. It is recommended that participants who experience a systemic hypersensitivity reaction be treated per the local standard of care.

### 8.3.7. Infusion-related Reactions

As with other mAbs, infusion-related reactions may occur during or following IV administration. If an infusion-related reaction occurs, additional data describing each symptom and sign should be provided to the sponsor in the CRF.

This table describes the location of infusion-related reaction information in this protocol.

| Topic | Location |
|---|---|

| | |
|---|---|
| Special treatment considerations | Section 6.1.1 |
| Premedication for infusions | Section 6.1.1.1 |
| Management of infusion reactions | Section 6.1.1.2 |
| DAIDS table describing severity | Section 6.1.1.2 |
| Treatment guidelines for infusion-related reactions | Section 6.1.1.2 |

Symptoms occurring during or after infusion of study intervention may also be defined according to AE categories such as acute allergic reaction (refer to DAIDS).

### 8.3.8. Product Complaints

A product complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a trial intervention. This may include reporting of any medication errors whether or not associated with an adverse event.

Sponsor collects product complaints on study intervention and drug delivery systems used in clinical studies in order to ensure the safety of study participants, monitor quality, and to facilitate process and product improvements.

Participants will be instructed to contact the investigator as soon as possible if they have a complaint or problem with the intervention so that the situation can be assessed.

NOTE: AEs/SAEs that are associated with a product complaint will also follow the processes outlined in Section 8.3.3 and Appendix 10.2 of the protocol.

**Time Period for Detecting Product Complaints**

Product complaints that result in an adverse event will be detected, documented, and reported to the sponsor during all periods of the study in which the intervention is used.

If the investigator learns of any product complaint at any time after a participant has been discharged from the study, and such incident is considered reasonably related to an intervention provided for the study, the investigator will promptly notify the sponsor.

**Prompt Reporting of Product Complaints to Sponsor**

Product complaints will be reported to the sponsor within 24 hours after the investigator becomes aware of the complaint.

The Product Complaint Form will be sent to the sponsor by a method designated by the sponsor.

**Follow-Up of Product Complaints**

Follow-up applies to all participants, including those who discontinue study intervention.

The investigator is responsible for ensuring that follow-up includes any supplemental investigations as indicated to elucidate the nature and/or causality of the product complaint.

New or updated information will be recorded on the originally completed form with all changes signed and dated by the investigator and submitted to the sponsor.

## 8.4. Treatment of Overdose

There is no known antidote for an overdose of bamlanivimab.

In the event of an overdose, the investigator should

1. contact the sponsor immediately
2. closely monitor the participant for any AE or SAE and laboratory abnormalities
3. provide supportive care as necessary, and
4. document the quantity of the excess dose in the CRF.

Decisions regarding infusion interruptions or modifications will be made by the investigator, in consultation with the sponsor, based on the clinical evaluation of the participant.

## 8.5. Pharmacokinetics

This section is not applicable for this study.

## 8.6. Pharmacodynamics

This section is not applicable for this study.

## 8.7. Genetics

This section is not applicable for this study.

## 8.8. Biomarkers

This section is not applicable for this study.

## 8.9. Immunogenicity Assessments

This section is not applicable for this study.

## 8.10. Health Economics

This section is not applicable for this study.

# 9. Statistical Considerations

## 9.1. Statistical Hypotheses

The null hypothesis is that the proportions of bamlanivimab-treated and control patients with COVID-19-related hospitalization by Day 29 will be similar.

## 9.2. Sample Size Determination

**Sample Size**

A sample size of at least 500 treated patients (and 500 control patients) will provide approximately 90% power to detect a treatment difference for the primary analysis, assuming the true rates of hospitalization are 12% in the control group and at most 6% in the treated group using a 2-sided 0.05 level analysis (accounting for 5% lost to follow up). For the exploratory subset analyses, a comparison of the effectiveness of treatment within multiple subsets based on age, comorbidities and other potential factors is of interest. A total sample size of 3000 in each group will provide at least 90% power under the same assumptions within each subgroup of interest, as long as the subset makes up at least 17% of the full population. This also assumes no multiplicity adjustment in the subset analyses.

A full discussion of power calculations will be provided in the SAP.

## 9.3. Populations for Analyses

This table defines the populations for analysis.

| Population | Description |
|---|---|
| Entered | All participants who sign the informed consent form. |
| Efficacy | All participants who received study intervention and provided at least one post-baseline measure for the relevant endpoint. Participants will be analyzed according to whether they received the study intervention (treated group, control group). |
| Safety | All participants who received study intervention. |

## 9.4. Statistical Analyses

The primary analysis is a comparison of rates of hospitalization for COVID-19 between treated patients and the control group in the Efficacy population. The pool of potential control patients will be obtained from patients in the EMR/claims data populations who meet the study entry criteria and would qualify for bamlanivimab treatment (but did not receive it). PS matching using risk factors associated with hospitalization for COVID-19 will be used to create a control group from the pool of potential control patients that provide balance with the treated patients on the relevant covariates. PS will be estimated for each patient in the bamlanivimab group and the comparator cohort by the logistic regression model, with treatment status as the dependent variable and the pre-defined independent variables considered as the potential confounders. For the PS matching process, each eligible patient receiving bamlanivimab will be matched to a control patient by a greedy 1:1 matching algorithm (D'Agostino 1998) with sampling without

replacement. The algorithm will utilize logit of PS with a caliper of 0.2 standard deviations of the logit of the PS (Austin 2014).

The success of the propensity score is judged by the balance in the confounder distributions it produces between the 2 study groups. Prior to initiating the outcome analysis, the quality of the PS adjustment and associated assumptions will be evaluated. The PS model will be finalized prior to initiating the analysis of the outcome measure.

The primary analysis will then be a comparison of the proportions of patients with a COVID-19-related hospitalization by Day 29 between the 2 treatment groups using a logistic regression model adjusting for variables a priori expected to be related to the outcome. Similarly, secondary analyses will include comparisons of the proportions of patients with COVID-19-related hospitalizations by Days 60 and 90, COVID-19-related ED visits, and COVID-19-related mortality through Days 29, 60, and 90 between the treatment groups, and will describe AEs and SAEs in bamlanivimab-treated patients. These details will be documented in the SAP prior to analysis.

### 9.4.1. Primary Endpoint

Proportion (percentage) of participants who experience COVID-19 related hospitalization (defined as ≥24 hours of acute care) or death by Day 29.

#### 9.4.1.1. Safety analysis

- COVID-19 related hospitalization, defined as ≥24 hours of acute care, up to Days 60 and 90
- ED visits for COVID-related causes
- AEs/SAEs

Safety analyses will be conducted using the safety population described in Section 9.3.

All investigational product and protocol procedure AEs will be listed, and if the frequency of events allows, safety data will be summarized using descriptive methodology.

The incidence of AEs will be presented by severity and by association with intervention as perceived by the investigator, regardless of ascertainment of relatedness.

Safety parameters that will be assessed include AEs and SAEs. The parameters will be listed and summarized using standard descriptive statistics.

### 9.4.2. Exploratory Analyses

Full details of the planned exploratory analyses will be described in the SAP and may include changes to the adjustment method such as dual matching to include both prognostic and propensity matching. E-value or other unmeasured confounding sensitivity analyses may also be included.

Additional exploratory analyses of the data will be conducted as deemed appropriate. Study results may be pooled with the results of other studies for safety.

### 9.4.3. Subgroup Analyses

This may not be powered for subgroup analyses; therefore, all subgroup analyses will be treated as exploratory.

Subgroup analyses may be conducted for the primary endpoint. Subgroups may include

- age
- sex
- race
- ethnicity
- baseline weight
- baseline body mass index
- concomitant medication
- various risk factors per EUA (see section 5.1)

More details on subgroup analyses will be outlined in the study SAP.

## 9.5. Interim Analyses

Not applicable

# 10. Supporting Documentation and Operational Considerations

## 10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

### 10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences International Ethical Guidelines
- applicable International Council for Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, and
- applicable laws and regulations.

The protocol, protocol amendments, ICF, IB, and other relevant documents (e.g., advertisements) must be submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study is initiated.

Any amendments to the protocol will require IRB/IEC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC
- notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures, and
- providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH guidelines, the IRB/IEC, European regulation 536/2014 for clinical studies (if applicable), and all other applicable local regulations.

Investigator sites are compensated for participation in the study as detailed in the CTA.

### 10.1.2. Financial Disclosure

Investigators and sub-investigators will provide the sponsor with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the study and for 1 year after the completion of the study.

### 10.1.3. Informed Consent Process

The investigator or his/her representative will explain the nature of the study, including the risks and benefits, to the participant or their legally authorized representative and answer all questions regarding the study.

Participants must be informed that their participation is voluntary. Participants or their legally authorized representative will be required to sign a statement of informed consent and child/adolescent assent, as appropriate, that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act requirements, where applicable, and the IRB/IEC or study center.

Due to strict respiratory isolation policies, limited access to COVID-19 patient rooms, and SARS-CoV-2 transmissibility via droplet-contaminated paper, verbal consent, and alternative methods of obtaining consent (e.g., by phone) will be allowed if approved by the IRB.

If a signed paper copy of the ICF or child/adolescent assent is allowed by site/institution policy, then the process of how it will be obtained and stored will need to be determined.

Any variation from the standard consent process due to isolation and infection control should be sent to the IRB for approval prior to enrollment. The site will document the process in their regulatory files and demonstrate that the process has IRB concurrence or approval.

The medical record must include a statement that written informed consent or child/adolescent assent (if deemed appropriate by local ethics review) was obtained before the participant was entered in the study and the date the written consent or assent was obtained. The authorized person obtaining the informed consent or child/adolescent assent, and, if applicable, the individual designated to witness a verbal consent, must also sign the ICF. The medical record should also describe how the investigator determined that the person signing the ICF was the participant's legally authorized representative (parent/guardian).

Participants and (when applicable) their legally acceptable representative, parent(s), or legal guardian must be re-consented to the most current version of the ICF(s) during their participation in the study, per the reconsenting guidelines as appropriate. Verbal reconsenting and alternative methods of obtaining consent may be utilized if approved by the IRB.

Minor participants must be re-consented if they reach the age of majority during the course of study, in order to continue participating.

A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative and is kept on file.

### 10.1.4. Data Protection

Participants will be assigned a unique identifier by the sponsor. Any participant records, datasets, or tissue samples that are transferred to the sponsor will contain the identifier only; participant names or any information which would make the participant identifiable will not be transferred.

The participant must be informed that their personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant who will be required to give consent for their data to be used as described in the informed consent.

The participant must be informed that their medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.

The sponsor has processes in place to ensure data protection, information security, and data integrity. These processes include appropriate contingency plan(s) for appropriate and timely response in the event of a data security breach.

### 10.1.5. Dissemination of Clinical Study Data

A clinical study report will be provided for this study and a summary of study information provided on publicly available websites.

### 10.1.6. Data Quality Assurance

**Investigator responsibilities**

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (e.g., laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

The investigator must maintain accurate documentation (source data) that supports the information entered in the CRF.

The investigator must permit study-related monitoring, audits, IRB/IEC review, and regulatory agency inspections and provide direct access to source data documents.

**Data monitoring and management**

The monitoring plan includes

- monitoring details describing strategy, for example, risk-based initiatives in operations and quality, such as Risk Management and Mitigation Strategies and Analytical Risk-Based Monitoring
- methods
- responsibilities and requirements
- handling of noncompliance issues, and
- monitoring techniques.

The sponsor or designee is responsible for the data management of this study including quality checking of the data. The sponsor assumes accountability for actions delegated to other individuals (e.g., Contract Research Organizations).

Study monitors will perform ongoing source data verification to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents. They will also ensure that the safety and rights of participants are being protected and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.

If on-site monitoring activities cannot occur, alternative measures will be used. Examples of alternative measures are use of technology for off-site monitoring or providing pseudonymized copies of source documents to the monitor electronically. The remote source data verification will be focused on critical efficacy data and important safety data.

**Records retention and audits**

Records and documents, including signed ICFs, pertaining to the conduct of this study must be retained by the investigator for the time period outlined in the CTA unless local regulations or institutional policies require a longer retention period.

No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor.

The sponsor or its representatives will periodically check a sample of the participant data recorded against source documents at the study site. The study may be audited by the sponsor or its representatives, and by regulatory agencies at any time. Investigators will be given notice before an audit occurs.

**Data capture system**

The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.

An EDC system will be used in this study for the collection of CRF data. The investigator maintains a separate source for the data entered by the investigator or designee into the sponsor-provided EDC system.

Only symptom assessments might be directly recorded by the investigator site personnel or a delegate into the EDC. The directly entered data will serve as source documentation. The investigator will not maintain an original, separate, written, or electronic record of these data. A certified copy of the respective data entry will be downloaded by the investigator for retention.

The investigator is responsible for the identification of any data to be considered source and for the confirmation that data reported are accurate and complete by signing the CRF.

Data collected via the sponsor-provided data capture systems will be stored at third parties. The investigator will have continuous access to the data during the study and until decommissioning of the data capture systems. Prior to decommissioning, the investigator will receive an archival copy of pertinent data for retention.

Data managed by a central vendor, such as laboratory test data, will be stored electronically in the central vendor's database system, and reports will be provided to the investigator for review and retention. Data will subsequently be transferred from the central vendor to the sponsor data warehouse.

Data from complaint forms submitted to sponsor will be encoded and stored in the global product complaint management system.

### 10.1.7. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator's site.

Data reported on the CRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Current medical records must be available.

The definition of what constitutes source data can be found in Section 10.1.6.

### 10.1.8. Study and Site Start and Closure

The study start date is the date on which the clinical study will be open for recruitment of participants.

**Site Closure**

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time, provided there is reasonable cause and enough notice is given in advance of the intended termination.

Reasons for the early closure of a study site by the sponsor or investigator may include but are not limited to

- failure of the investigator to comply with the protocol, the requirements of the IRB/IEC or local health authorities, the sponsor's procedures, or GCP guidelines
- inadequate recruitment of participants by the investigator, or
- discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the IECs/IRBs, the regulatory authorities, and any contract research organization(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participants and assure appropriate participant therapy and/or follow-up.

### 10.1.9. Publication Policy

In accordance with the sponsor's publication policy, the results of this study will be submitted for publication by a peer-reviewed journal if the results are deemed to be of significant medical importance.

### 10.1.10. Investigator Information

Physicians with specialties, including, but not limited to infectious disease, acute or critical care, pulmonary disease, immunology, or other appropriate specialties may participate as investigators.

### 10.1.11. Long-Term Sample Retention

Not applicable

## 10.2. Appendix 2: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting

### 10.2.1. Definition of AE

**AE Definition**

- An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention.
- NOTE: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

**Events Meeting the AE Definition**

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (e.g., ECG, radiological scans, and vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator (i.e., not related to progression of underlying disease).
- Exacerbation of a chronic or intermittent preexisting condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdose should be reported regardless of sequelae.
- "Lack of efficacy" or "failure of expected pharmacological action" per se will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. However, the signs, symptoms, and/or clinical sequelae resulting from lack of efficacy will be reported as AE or SAE if they fulfill the definition of an AE or SAE.

**Events NOT Meeting the AE Definition**

- The following study-specific clinical events related to COVID-19 are exempt from adverse event reporting unless the investigator deems the event to be related to the administration of study intervention:
  - hypoxemia due to COVID-19 requiring supplemental oxygen
  - hypoxemia due to COVID-19 requiring non-invasive ventilation or high flow oxygen devices, and

- respiratory failure due to COVID-19 requiring invasive mechanical ventilation or ECMO.

- Any clinically significant abnormal laboratory findings or other abnormal safety assessments which are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.
- The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition.
- Medical or surgical procedure (e.g., endoscopy and appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).
- Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

### 10.2.2. Definition of SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met (e.g., hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

**An SAE is defined as any untoward medical occurrence that, at any dose:**

**a. Results in death**

**b. Is life-threatening**

The term "life-threatening" in the definition of "serious" refers to an event in which the participant is at risk of death at the time of the event. It does not refer to an event, which hypothetically might have caused death, if it were more severe.

**c. Requires inpatient hospitalization or prolongation of existing hospitalization**

- In general, hospitalization signifies that the participant has been admitted to hospital for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.
- Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.

**d. Results in persistent disability/incapacity**

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.

- This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle), which may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

**e. Is a congenital anomaly/birth defect**

**f. Other situations:**

- Medical or scientific judgment should be exercised in deciding whether SAE reporting is appropriate in other situations such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent 1 of the other outcomes listed in the above definition. These events should usually be considered serious.
- Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

### 10.2.3. Recording and Follow-Up of AE and/or SAE

**AE and SAE Recording**

- When an AE or SAE occurs, it is the responsibility of the investigator to review all documentation (e.g., hospital progress notes, laboratory reports, and diagnostics reports) related to the event.
- The investigator will then record all relevant AE or SAE information in the CRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records to Sponsor or designee in lieu of completion of the AE or SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by Sponsor or designee. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Sponsor or designee.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE or SAE.

**Assessment of Intensity**

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories, which together with serious (i.e., SAE) criteria on the AE CRF ("results in death" and "life-threatening"), are aligned with the DAIDS Table for Grading the Severity of Adult and Pediatric Adverse Events, version 2.1 (July 2017).

**Mild:** Mild symptoms causing no or minimal interference with usual social and functional activities, with intervention not indicated.

**Moderate:** Moderate symptoms causing greater than minimal interference with usual social and functional activities, with intervention indicated.

**Severe:** Severe symptoms causing inability to perform usual social and functional activities, with intervention or hospitalization indicated.

An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

**Assessment of Causality**

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE or SAE.
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- The investigator will use clinical judgment to determine the relationship.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration will be considered and investigated.
- The investigator will also consult the IB and/or Product Information, for marketed products, in his or her assessment.
- For each AE or SAE, the investigator **must** document in the medical notes that he or she has reviewed the AE or SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to Sponsor or designee. However, it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to Sponsor or designee.
- The investigator may change his or her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is 1 of the criteria used when determining regulatory reporting requirements.

**Follow-Up of AEs and SAEs**

- The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by Sponsor or designee to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

- If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide Sponsor or designee with a copy of any postmortem findings including histopathology.
- New or updated information will be recorded in the originally completed CRF.
- The investigator will submit any updated SAE data to Sponsor or designee within 24 hours of receipt of the information.

### 10.2.4. Reporting of SAEs

**SAE Reporting via an Electronic Data Collection Tool**

- The primary mechanism for reporting an SAE will be the electronic data collection tool.
- If the electronic system is unavailable, then the site will use the paper SAE data collection tool (see next section) in order to report the event within 24 hours.
- The site will enter the SAE data into the electronic system as soon as it becomes available.
- After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data.
- If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to the sponsor by telephone.
- Contacts for SAE reporting can be found in site training documents.

**SAE Reporting via Paper CRF**

- Facsimile transmission of the SAE paper CRF is the preferred method to transmit this information to the sponsor.
- Initial notification via telephone does not replace the need for the investigator to complete and sign the SAE CRF pages within the designated reporting time frames.
- Contacts for SAE reporting can be found in site training documents.

### 10.2.5. Medication Error

FDA defines medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of a healthcare provider, patient, or consumer (FDA 2020b).

## 10.3. Appendix 3: Contraceptive Guidance and Collection of Pregnancy Information

**Definitions:**

**Women**

**Woman of Childbearing Potential**

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (e.g., amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before first dose of study intervention, additional evaluation should be considered.

**Woman not of Childbearing Potential**

Women in the following categories are not considered women of childbearing potential:

1. premenarchal
2. premenopausal female with either
    a. documented hysterectomy
    b. documented bilateral salpingectomy, or
    c. documented bilateral oophorectomy.

For individuals with permanent infertility due to an alternate medical cause other than the above, (e.g., Müllerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

Note: Determination can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview.

3. Postmenopausal female is defined as, women with:
    d. 12 months of amenorrhea for women >55, with no need for FSH
    e. 12 months of amenorrhea for women >40 years old with FSH ≥40 mIU/mL and no other medical condition such as anorexia nervosa and not taking medications during the amenorrhea (e.g., oral contraceptives, hormones, gonadotropin releasing hormone, anti-estrogens, selective estrogen receptor modulators (SERMs), or chemotherapy that induced amenorrhea)

**Participation in the Study**

Women of child-bearing potential and not of child-bearing potential may participate in this study.

Women of child-bearing potential must test negative for pregnancy prior to initiation of treatment as indicated by a negative urine pregnancy test at the screening visit.

Women of child-bearing potential who are completely abstinent or in a same sex relationship, as part of their preferred and usual lifestyle, must agree to either remain abstinent or stay in a same sex relationship without sexual relationships with males.

All other women of child-bearing potential must agree to use 2 forms of effective contraception, where at least one form is highly effective (less than 1% failure rate), for the entirety of the study.

Abstinence or contraception must continue for 90 days after the last dose of intervention.

**Acceptable Methods of Contraception**

Highly effective methods of contraception (less than 1% failure rate) comprise but are not limited to

- combination oral contraceptives
- implanted contraceptives, or
- intrauterine devices.

Effective methods of contraception comprise but are not limited to diaphragms with spermicide or cervical sponges.

**Not Acceptable Methods of Contraception**

Use of male and female condoms as a double barrier method is not considered acceptable due to the high failure rate when these barrier methods are combined.

Barrier protection methods without concomitant use of a spermicide are not an effective or acceptable method of contraception.

Periodic abstinence (e.g., calendar, ovulation, symptothermal, post-ovulation methods), declaration of abstinence just for the duration of a trial, and withdrawal are not acceptable methods of contraception.

**Men**

Men, regardless of their fertility status, must agree to either remain abstinent (if this is their preferred and usual lifestyle) or use condoms as well as one additional highly effective method of contraception (less than 1% failure rate) or effective method of contraception with non-pregnant women of child bearing potential partners for the duration of the study and until their plasma concentrations are below the level that could result in a relevant potential exposure to a possible fetus, predicted to be 90 days after the last dose.

Men with pregnant partners should use condoms during intercourse for the duration of the study and until the end of estimated relevant potential exposure to the fetus, predicted to be 90 days after the last dose.

**Acceptable Methods of Contraception**

Highly effective methods of contraception (less than 1% failure rate) comprise, but are not limited to

- combination oral contraceptives
- implanted contraceptives, or
- intrauterine devices.

Effective methods of contraception comprise but are not limited to diaphragms with spermicide or cervical sponges.

Men and their partners may choose to use a double-barrier method of contraception that must include use of a spermicide.

**Other Guidance**

Men should refrain from sperm donation for the duration of the study and until their plasma concentrations are below the level that could result in a relevant potential exposure to a possible fetus, predicted to be 90 days after the last dose.

**Collection of Pregnancy Information**

**Male participants with partners who become pregnant**

The investigator will attempt to collect pregnancy information on any male participant's female partner who becomes pregnant while the male participant is in this study. This applies only to male participants who receive study intervention.

After obtaining the necessary signed informed consent and assent (if applicable) from the pregnant female partner directly, the investigator will record pregnancy information on the appropriate form and submit it to the sponsor within 24 hours of learning of the partner's pregnancy.

The female partner will also be followed to determine the outcome of the pregnancy. Information on the status of the mother and child will be forwarded to the sponsor. Generally, this information will include a follow-up of at least 5 half-lives after last exposure or birth. Any termination of the pregnancy will be reported including fetal status (presence or absence of anomalies) and indication for the procedure.

**Female participants who become pregnant**

The investigator will collect pregnancy information on any female participant who becomes pregnant while participating in this study. The initial information will be recorded on the appropriate form and submitted to the sponsor within 24 hours of learning of a participant's pregnancy.

The participant will be followed to determine the outcome of the pregnancy. The investigator will collect follow-up information on the participant and the neonate and the information will be forwarded to the sponsor. Generally, this information will include a follow-up of at least 5 half-lives after last exposure or birth. Any termination of pregnancy will be reported, including fetal status (presence or absence of anomalies) or indication for the procedure.

While pregnancy itself is not considered to be an AE or SAE, any pregnancy complication or elective termination of a pregnancy for medical reasons will be reported as an AE or SAE.

A spontaneous abortion (occurring at <20 weeks gestational age) or still birth (occurring at >20 weeks gestational age) is always considered to be an SAE and will be reported as such.

Any post-study pregnancy-related SAE considered reasonably related to the study intervention by the investigator will be reported to the sponsor as described in Section 8.3.4. While the

investigator is not obligated to actively seek this information in former study participants, he or she may learn of an SAE through spontaneous reporting.

## 10.4. Appendix 4: Abbreviations

| Term | Definition |
|---|---|
| **AC** | Assessment committee |
| **ADA** | Anti-drug antibody |
| **AE** | Adverse event |
| **ADE** | Antibody-dependent enhancement |
| **Assent** | Agreement from a child or other individual who is not legally capable of providing consent, but who can understand the circumstances and potential risks involved in participating in a study. |
| **BMI** | Body mass index |
| **Complaint** | A complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, purity, durability, reliability, safety or effectiveness, or performance of an intervention. |
| **Compliance** | Adherence to all study-related, good clinical practice (GCP), and applicable regulatory requirements. |
| **CRF** | Case report form |
| **CRP** | Clinical research physician: individual responsible for the medical conduct of the study. Responsibilities of the CRP may be performed by a physician, clinical research scientist, global safety physician, or other medical officer. |
| **CTA** | Clinical trial agreement |
| **DAIDS** | Division of AIDS |
| **DMC** | Data monitoring committee |
| **ECG** | Electrocardiogram |
| **ED** | Emergency department |
| **EDC** | Electronic data capture |
| **EMR** | Electronic medical record |
| **Enroll** | The act of assigning a participant to a treatment. Participants who are enrolled in the study are those who have been assigned to a treatment. |
| **Enter** | Participants entered into a study are those who sign the informed consent form directly or through their legally acceptable representatives. |
| **EUA** | Emergency Use Authorization |
| **FiO2** | Fraction of inspired oxygen in the air |

| | |
|---|---|
| **GCP** | Good clinical practice |
| **IB** | Investigator's Brochure |
| **ICF** | Informed consent form |
| **ICH** | International Council for Harmonisation |
| **IMP** | Investigational Medicinal Product |
| **Informed consent** | A process by which a participant voluntarily confirms his or her willingness to participate in a particular study, after having been informed of all aspects of the study that are relevant to the participant's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form. |
| **Interim analysis** | An interim analysis is an analysis of clinical study data, separated into treatment groups, that is conducted before the final reporting database is created/locked. |
| **Intervention** | A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including products already on the market when used or assembled (formulated or packaged) in a way different from the authorized form, or marketed products used for an unauthorized indication, or marketed products used to gain further information about the authorized form. |
| **IRB/IEC** | Institutional Review Boards/Independent Ethics Committees |
| **IV** | Intravenous |
| **IWRS** | Interactive web-response system |
| **Legal representative** | An individual or judicial or other body authorized under applicable law to consent, on behalf of a prospective participant, to their participation in the clinical study. |
| **Medication error** | A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of a healthcare provider, patient, or consumer (FDA 2020b). |
| **Mabs** | Monoclonal antibodies |
| **NP** | Nasopharyngeal |
| **Participant** | Equivalent to CDISC term "subject": an individual who participates in a clinical trial, either as recipient of an investigational medicinal product or as a control |
| **PK/PD** | Pharmacokinetics/pharmacodynamics |
| **PS** | Propensity score |
| **SAE** | Serious adverse event |
| **SAP** | Statistical analysis plan |
| **SARS** | Severe acute respiratory syndrome |

| | |
|---|---|
| **Screen** | The act of determining if an individual meets minimum requirements to become part of a pool of potential candidates for participation in a clinical study. |
| **SpO2** | Saturation of peripheral oxygen |

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**Leo Document ID = 8ac6f859-6b0b-4bf6-8d30-2c0017eaee3f**

**Approver:** PPD

**Approval Date & Time: 18-Dec-2020 23:02:04 GMT**

**Signature meaning: Approved**

**Approver:** PPD

**Approval Date & Time: 18-Dec-2020 23:42:05 GMT**

**Signature meaning: Approved**